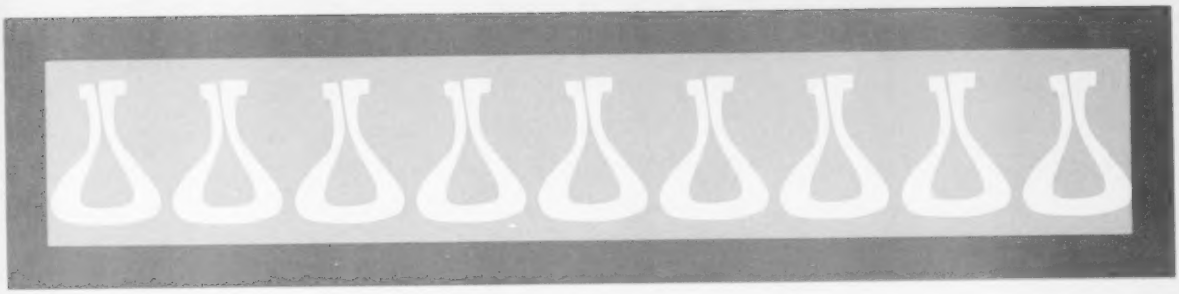

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PSYCHOPHARMACOLOGY ABSTRACTS

NATIONAL INSTITUTE OF MENTAL HEALTH

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Volume 12, Number 2 October 1974

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Carrie Lee Rothgeb, *Editor*
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ABSTRACTS

PRECLINICAL PSYCHOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

174967 Granchelli, Felix Edward. Northeastern University, Boston, MA **Synthesis of hydroxyaporphines as potential antiparkinsonian agents. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 73-4647 HC$10.00 MF$4.00 173 p.

A synthesis of hydroxyaporphines as potential antiparkinson agents is presented. Synthesis of 11-hydroxyaporphines were carried out via the Heissert alkylation-Pachorr cyclization route, and synthesis of the 7-hydroxyaporphines and the 6, 7-dehydronoraphorphine were carried out by a novel synthetic sequence. The techniques used resulted in total synthesis of 7-hydroxyaporphines. An oxazalone ring preserved an hydroxyl function in a sensitive position of a dihydrophenanthrene like structure. The compounds were evaluated in rats which had a unilateral lesion of the nigra-striatal dopamine neurones, produced by 6-hydroxydopamine. When apomorphine was administered, rotation by the rat was induced toward the intact side. The 7- and 11-hydroxyaporphines demonstrated similar but somewhat weaker dopamine receptor stimulating activity. (Journal abstract modified)

180098 Moracci, Franco Micheletti; Liberatore, Felice; Marchini, Paolo; Liso, Gaetano; Cardellini, Mario. Institute of Applied Pharmaceutical Chemistry, Univ. of Rome, Rome, Italy **Synthesis and pharmacological properties of 5a,6,7,8,9,10,10a, 11-octahydrobenzo(b)cyclohepta(e)-(1,4)thiazine derivatives.** Journal of Medicinal Chemistry. 17(4):463-465, 1974.

The synthesis of a number of octahydro(b)cyclohepta(e)(1,4)thiazines was carried out in order to study the variations of pharmacological activity related to reduction and homologation of one of the aromatic rings of phenothiazine. The results of in vitro testing indicates that antihistaminic activity was very modest. The test compounds had low antiacetylcholine effects. The data suggest modest interference with coordination of motor activity and muscle tone. The substances failed to antagonize reserpine, to potentiate barbiturate effects and to modify the spontaneous motor activity. 19 references. (Author abstract modified).

180487 Terada, Atsusuke; Yabe, Yuichiro; Miyadera, Tetsuo; Tachikawa, Ryuji. Research Laboratories, Sankyo Co., Ltd., Tokyo, Japan **Studies on benzodiazepinooxazoles. III. Reactions and rearrangements of benzo(6,7)-1,4-diazepino(5,4-b)-oxazole derivatives.** Annual Report of Sankyo Research Laboratories (Tokyo). 25:174-175, 1973.

A mechanistic assumption for the formation of exo-methylene compounds and isoindoles and acridanone derivatives from reactions and rearrangements of benzo(6,7)-1,4-diazepino(5,4-b)-oxazole derivatives is given. Treatment of 10-halogeno-2,3,5,6,7,11b-hexahydro-7-methyl-11b-phenylbenzo(6,7)-1,4- diazepino(5,4-b)oxazol-6-one with dimethyl formamide in the presence of sodium hydride gave exo-methylene compounds. On the other hand, the compounds having halogen at the o-position of the 11b-phenyl group gave no exo-methylene compounds, but isoindoles and acridanone derivatives. (Author abstract)

180488 Terada, Atsusuke; Yabe, Yuichiro; Miyadera, Tetsuo; Tachikawa, Ryuji. Research Laboratories, Sanyko Co., Ltd., Tokyo, Japan **Studies on benzodiazepinooxazoles. IV. The formation of quinolones by the ring contraction of a benzo(6,7)-1,4-diazepino(5,4-b)oxazole derivative.** Annual Report of Sankyo Research Laboratories (Tokyo). 25:175-176, 1973.

A mechanistic assumption for the formation of 6-chloro-3-(2-hydroxyethyl)-1-methyl-4-phenyl-2(1H)-quinolone by the ring contraction of a benzo(6,7)-1,4-diazepino(5,4-b)oxazole derivative is presented. Treatment of 10-chloro-2,3,5,6,7,11b-hexahydro-7-methyl-11b-phenylbenzo(6,7)-1,4-diazepino(5,4-b)oxazol-6-one with sodium hydride in dimethyl acetamide gave the two compounds 6-chloro-3-(2-hydroxyethyl)-1-methyl-4-phenyl-2(1H)- quinolone and 6-chloro-3-hydroxy-1-methyl-4-phenyl-2(1H)-quinolone. (Author abstract)

180489 Terada, Atsusuke; Yabe, Yuichiro; Miyadera, Tetsuo; Tachikawa, Ryuji. Research Laboratories, Sankyo Co., Ltd., Tokyo, Japan **Studies on benzodiazepinooxazoles. V. Reactions of benzo(6,7)-1,4-diazepino(5,4-b)oxazole derivatives with acetic anhydride.** Annual Report of Sanyko Research Laboratories (Tokyo). 25:176-177, 1973.

Treatment of benzo(6,7)-1,4-diazepino(5,4-b)oxazole derivatives with acetic anhydride and pyridine gave six isoindole compounds with ring contraction. A plausible mechanism of the reaction and the physical properties of these products are presented. (Author abstract)

180670 Turner, Carlton E.; Hadley, Kathy W.; Davis, Kenneth H., Jr. Research Institute of Pharmaceutical Sciences, School of Pharmacy, University, MS 38677 **Constituents of Cannabis sativa L. V.: Stability of an analytical sample extracted with chloroform. (Unpublished paper).** University, MS, University of Mississippi, 1973. 14 p.

The stability of an analytical sample of cannabis sativa extracted with chloroform was studied. Chloroform extracts of Cannabis sativa L. are stable for a period of 144 hours. When compared to seven other solvents (benzene, pentane, hexane, pet ether, ethanol, acetone, and ethyl ether), chloroform was the solvent of choice for extracting delta9-tetrahydrocannabinol from plant material. Additionally, chloroform extracts can be used to analyze for neutral cannabinoids or for their carboxylate acid derivatives. 12 references. (Author abstract modified)

180739 Krunnfusz, Robert William. University of Iowa **Synthetic studies leading toward the preparation of linear benzoquinolines. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, Mich., Univ. M-films, No. 73-13567 HC$10.00 MF$4.00 86 p.

Several synthetic methods to prepare one of the linear benzoquinolines, 6,7-dimethoxy-10-methylbenzo(g)quinoline, as part of a continuing study of structure activity relationships of centrally acting emetics and anti-Parkinsonian compounds are presented. An improved method of preparing 1-methyl-5,6-dimethoxy-2(1H)-naphthalenone was accomplished. A convenient method was investigated for the conversion of 2-tetralones to 2-naphthols, and this method was used to prepare 1-methyl-2-naphthol, 1-methyl-6-methoxy-2-naphthol, and 1-methyl-5,6-dimethoxy-2-naphthol. The Bucherer reaction was investigated for the preparation of 1-methyl-2-naphthylamines from the corresponding naphthols. The Bucherer reaction was successfully employed in the preparation of 1-methyl-2-naphthylamine and 1-methyl-6-methoxy-2-naphthylamine. A new approach to the synthesis of 2-naphthylamines from 2-naphthols with 4-chloro-2-phenylquinazoline was studied. 2-Naphthylamine was successfully prepared from 2-naphthol with this reagent. (Journal abstract modified)

181391 Wiley, Robert A. University of Kansas, Lawrence, KS **Psychopharmacological agents: stereochemical studies.** Psychopharmacology Bulletin. 10(1):63-64, 1974.

Studies aimed at precise definition of the chemical requirements for optimum tranquilizer and antidepressant potency for a series of closely related compounds are outlined. The amitriptyline compounds and chlorprothixene derivatives are synthesized. Preliminary results include the preparation of a 2-chlorodibenzocycloheptadiene-5-one, which was checked against a prepared model, dibenzyl suberone, by spectral means. Preparation of the phenotiazine series has progressed to 2-chloro-10-thiaxanthenone. 3-Dimethylaminocyclohexanole was prepared by a reduction of the corresponding phenol with a rhodium catalyst. A new bromide with a low yield was prepared; and a tetracyclic material was constructed which should yield the desired tricylcic ketone. A new chromatographic method yielded pure cis-isomers and trans-isomers of chlorprothixene.

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

177099 Saji, Yoshiaki; Mizuno, Kiyofumi; Nagawa, Yuji. Takeda Research Laboratories, Osaka, Japan **Anticonvulsive activity of 8-chloro-6-phenyl-4H-S-triazolo (4,3-a)(1,4)benzodiazepine (D-40TA) and its effect on limbic system.** Journal of the Takeda Research Laboratories (Osaka). 32(2):172-180, 1973.

The effects of a new central nervous system depressant, 8-chloro-6-phenyl-4H-s-triazolo(4,3-a)(1,4)benzodiazepine (D-40TA) on the seizure induced by electroshock on various chemical convulsants in mice and on the electroencephalographic after discharge induced by stimulation of the cortex, thalamus and limbic structures in cats with chronically implanted electrodes were studied. Results suggest that D-40TA might be useful for therapy for a petit mal epilepsy as well as psychomotor seizure in man. Findings indicate that its hypnogenic and psychosedative effect may be due to the depression of excitability of the limbic system as well as the hypothalamus. 15 references. (Author abstract modified)

180490 Miyadera, Tetsuo; Kawano, Yoichi; Terada, Atsusuke; Kamioka, Toshiharu; Takagi, Hiromu; Tachikawa, Ryuji. Research Laboratories, Sankyo Co., Ltd., Tokyo, Japan **Studies on benzodiazepinooxazoles. VI. Synthesis and pharmacology of 11b-pyridyl and 11b-thienyl derivatives of benzodiazepinooxazoles.** Annual Report of Sankyo Research Laboratories (Tokyo). 25:69-72, 1973.

Synthesis and pharmacology of 11b-pyridyl and 11b-thienyl derivatives of benzodiazepinooxazoles were examined in a study of tricyclic minor tranquilizers. The pharmacological test with mice showed that all the pyridyl compounds have much more potent antibemegride activity than the thienyl derivatives, but a little weaker activity compared with the corresponding 11b-phenyl analogs. Specific data are given on 2-(2-bromoacetamido-5-chlorobenzoyl)pyridine and 10-chloro-2-methyl-2,3,5,6,7,11b-hexahydro-11b-(2-pyridyl)benzo(6,7)-1 4- diazepino(5,4,-b)oxazol-6-one. 4 references.

181657 Take, Yomei; Ikeda, Katsuichi; Nagawa, Yuji. Takeda Chemical Industries, Ltd., Osaka, Japan **Effect of 8-chloro-6-phenyl-4H-s-triazo (4,3-a)(1,4)-benzodiazepine (D-40TA) on the daytime sleep-wakefulness patterns in monkeys.** Journal of the Takeda Research Laboratories (Osaka). 32(3):289-298, 1973.

The effect of 8-chloro-6-phenyl-4H-s-triazolo(4,3-a) (1,4)-benzodiazepine (D-40TA) on the daytime sleep - wakefulness cycle in Japanese monkeys with chronically implanted electrodes was studied in comparison with nitrazepam. A single oral dose of D-40TA at 0.25-4mg/kg and nitrazepam at 0.375-6mg/kg caused a clearly dose dependent increase in the sleeping state with a markedly dominant appearance of the slow electroencephalogram activities in all leads. The hypnotic potency of D-40TA was approximately 1.5-10 times that of nitrazepam. As compared with nitrazepam, the hypnotic effect of D-40TA was characterized by rapid establishment of the more stable sleeping state which decayed more rapidly after a dose dependent persistence with less alternation of the sleep - wakefulness cycles. Chronic 14 day studies of the hypnotic action of D-40TA provided no evidence to suggest the development of tolerance or accumulation. 9 references. (Author abstract modified)

181658 Take, Yomei; Fukuda, Naohisa; Nagawa, Yuji. Takeda Chemical Industries, Ltd., Osaka, Japan **Effect of 8-chloro-6-phenyl-4H-s-triazolo(4,3-a) (1,4)-benzodiazepine (D-40TA) on the daytime sleep-wakefulness patterns in normal and p-chlorophenylalanine-isomnic cats.** Journal of the Takeda Research Laboratories (Osaka). 32(3):275-288, 1973.

The effects of 8-chloro-6-phenyl-4H-s-triazolo(4,3-a) 1,4)-benzodiazepine (D - 40TA) on the sleep-wakefulness cycle in normal state and in p-chlorophenylalanine (PCPA) induced insomnia in cats with chronically implanted electrodes were studied in comparison with the effects of nitrazepam. D-40TA given orally at 0.125-2mg/kg caused an increase in the total waking time due to prolongation of one waking period in the normal state. These doses also decreased the slow wave sleep (SWS) and particularly the paradoxical sleep (PS). Atypical PS (APS) consisted of electroencephalogram (EEG) patterns different from those in normal PS and with slow or no eye movement. Low spinal transection disclosed a hypnotic action of D-40TA by induction of SWS consisting predominantly of cortical spindle bursts. This suggests that generation of the activating impulses to adjust the posture impaired by muscle relaxation disturbs in part a sleep inducing effect of D-40TA in normal cats. 29 references. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

175230 MacInnes, J. W.; Luttges, M. W. Institute for Behavioral Genetics, University of Colorado, Boulder, CO 80302 **Interactive effects of cycloheximide and puromycin in altering brain polyribosomes and neural and behavioural responses to electroshock in mice.** Journal of Neurochemistry (Oxford). 21(4):775-781, 1973.

Interactive effects of puromycin and cycloheximide on brain polyribosomes and cortical electrical activity were investigated in mice. The time courses of action of the drugs on these parameters, in comparison to their inhibitory actions on protein synthesis, were also observed. The results indicate that the disruption of brain polyribosomes by cycloheximide was independent of its inhibition of protein synthesis, whereas the two processes were closely linked in the case of puromycin. For both the disruption of polyribosomes and the alteration of electrical activity, the order in which the drugs were administered was critical, with preadministration of cycloheximide having a protective effect. In con-

trast to the massive effect of cycloheximide on brain polyribosomes, the drugs had no such effect on polyribosomes from liver. 17 references. (Author abstract)

175232 Bronaugh, R. L.; Erwin, V. Gene. Department of Pharmacology, University of Colorado Medical Center, Denver, CO 80220 **Partial purification and characterization of NADPH-linked aldehyde reductase from monkey brain.** Journal of Neurochemistry (Oxford). 21(4):809-815, 1973.

The activity of NADPH linked aldehyde reductase in various regions of monkey brain was determined in vitro. The highest specific activity of the enzyme was found in areas of the brainstem; including the pons, medulla and midbrain. The aldehyde metabolites of the biogenic amines, norepinephrine, serotonin, dopamine and octopamine, were readily reduced by the NADPH linked aldehyde reductase. The maximum velocity for 3,4-dihydroxyphenylglycolaldehyde was, respectively, five fold or three fold greater than that determined for 3,4-dihydroxyphenylacetaldehyde or 5-hydroxyindoleacetaldehyde. The highly purified enzyme derived from monkey brain was markedly inhibited by barbiturates, diphenylhydantoin, and chlorpromazine, but not by pyrazole. From data obtained by sucrose density gradient centrifugation and Sephadex chromatography the molecular weight of aldehyde reductase was determined to be about 70,000 daltons. 18 references. (Author abstract modified)

175233 Horn, A. S. MRC Neurochemical Pharmacology Unit, Department of Pharmacology, University of Cambridge Medical School, Cambridge, England **Structure activity relations for the inhibition of 5-HT uptake into rat hypothalamic homogenates by serotonin and tryptamine analogues.** Journal of Neurochemistry (Oxford). 21(4):883-888, 1973.

Various 5-hydroxytryptamine (5-HT) and tryptamine analogues were examined as inhibitors of (3H)5-HT uptake into rat hypothalamic homogenates. Acetylation of the terminal amino group or methylation of the hydroxyl group of 5-HT resulted in compounds having a reduced affinity for the serotonin uptake site. This also occurred when the hydroxyl group of 5-HT was substituted in other positions on the benzene ring. Substitution of the tryptamine side chain in the alpha-position by methyl or ethyl groups, but not by a carboxyl function, enhanced the affinity for the 5-HT uptake site. Increasing the tryptamine side chain by one carbon atom also resulted in a more potent compound. Several of the compounds tested are known to be either hallucinogens or antidepressants. 23 references. (Author abstract)

175238 Karler, Ralph; Cely, William; Turkanis, Stuart A. Department of Pharmacology, University of Utah School of Medicine, Salt Lake City, UT 84132 **The anticonvulsant activity of cannabidiol and cannabinol.** Life Sciences. 13(11):1527-1531, 1973.

The anticonvulsant activity of delta9-tetrahydrocannabinol (THC) was compared with that of two other naturally occurring cannabinoids, cannabidiol and cannabinol, in a maximal electroshock test in mice. The drugs were administered as an emulsion of sesame seed oil, Tween 80 and saline to mice. The results indicate that all three cannabinoids are effective anticonvulsants. The time for peak effect is about 2 hr. In terms of relative potencies, cannabidiol and delta9-THC are similar but both of them are more active than cannabinol. 15 references. (Author abstract)

175239 Oreland, Lars; Kinemuchi, Hiroyasu; Yoo, Bong Y. Department of Pharmacology, University of Umea, S-901 87 Umea, Sweden **The mechanism of action of the monoamine oxidase inhibitor pargyline.** Life Sciences (Oxford). 13(11):1533-1541, 1973.

The mechanism of action of the monoamine oxidase inhibitor pargyline was examined in purified pig liver. Monoamine oxidase, which has been shown to contain one mole of covalently bound FAD per mole of enzyme, was inhibited by (14C) pargyline (N-methyl-N-2-(propynyl)-benzylamine) and then extensively degraded by pronase. The pargyline containing fragment was purified by gel filtration and ion exchange chromatography. The equimolar ratio between pargyline and flavin was retained after the purification. Thin layer chromatography in several systems showed that pargyline was bound to the flavopeptide. Amino acid analyses of the peptide yielded cysteic acid, aspartic acid, serine and glycine in a molar ratio of 1:1:1:2. 11 references. (Author abstract)

175240 Korduba, C. A.; Veals, J.; Symchowicz, S. Department of Biochemistry, Schering Corporation, Bloomfield, NJ 07003 **The effect of pheniramine and its structural analogues on 5-**

hydroxytryptamine in rat and mouse brain. Life Sciences (Oxford). 13(11):1557-1564, 1973.

A series of pheniramine analogues were tested for the ability to inhibit 5-hydroxytryptamine(5-HT) uptake by synaptosomes of rat corpus striatum. A chlorine or bromine substitution on the aromatic ring greatly facilitated the inhibitory activity of pheniramine. 3,4-Dichlorpheniramine was found to be the most active in this series and was also more effective than desipramine or amphetamine. In mice treated with 3,4-dichlorpheniramine, the rate of 5-HT synthesis in brain tissue was considerably reduced when compared to controls. 14 references. (Author abstract)

175241 Fibiger, Hans C.; McGeer, Edith G. Division of Neurological Sciences, Department of Psychiatry, University of British Columbia, Vancouver, Canada **Increased axoplasmic transport of H3-dopamine in nigro-neostriatal neurons after reserpine.** Life Sciences (Oxford). 13(11):1565-1571, 1973.

Increased axoplasmic transport of 3H-dopamine in the nigro-neostriatal neurons after reserpine in rats is reported. The activity recovered from the substantia nigra was significantly reduced by reserpine pretreatment however. Stereotaxic injection of 14C-leucine into the substantia nigra indicated that neither fast nor slow axoplasmic transport of protein was influenced by reserpine pretreatment in these same neurons. The increased transport of dopamine appears therefore to be due to a relatively selective action of reserpine. The results suggest that reserpine either increases the binding of dopamine to newly synthesized amine storage granules, increases the number of newly synthesized amine storage granules, or accelerates the rate of transport of amine storage granules. The results support the view that reserpine can increase the membrane permeability of adrenergic neurons to the outward movement of catecholamines. 9 references. (Author abstract modified)

175650 Beattie, Craig W.; Schwartz, Neena B. Bioanalytical Dept., Pharmaceutical Division, Pennwalt Corporation, Rochester, NY 14603 **Blockade of the proestrous LH surge in cyclic rats by barbiturate administration on diestrus.** Proceedings of the Society for Experimental Biology and Medicine. 142(3):933-935, 1973.

A study was made of ovulation and a blockade of the proestrous LH surge in cyclic 4 day rats by barbiturate administration at 1330 hr of diestrus. Uterine ballooning was not blocked in the majority of animals injected with pentobarbital. These results suggest that barbiturates, administered in the early afternoon on any day of the estrous cycle of the 4 day rat, inhibit ovulation by a central block of LH release. 14 references. (Author abstract modified)

175751 Wursch, M. S.; Otis, L. S.; Green, D. E.; Forrest, I. S. Department of Psychiatry, Stanford University School of Medicine, Stanford, CA **3H-delta-9-tetrahydrocannabinol (THC) metabolism in Rhesus and Squirrel monkeys.** Proceedings of the Western Pharmacological Society. 15:68-73, 1972.

A suitable primate model for the in vivo metabolism of delta9-tetrahydrocannabinol (THC) on which the biotransformations could be studied was determined. The data for gross urinary and fecal elimination of 3H-delta9-THC in Squirrel monkeys indicated that this species is not a suitable primate model. The corresponding data for the Rhesus monkey were similar to those for man. A methodology for the assay of THC metabolites is described, and it is concluded that different unknown metabolites constitute the majority of the THC derivatives. 8 references.

175759 Callery, Patrick S.; Zweig, Jonathan S.; Castagnoli, Neal, Jr. Department of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, CA 94122 **Stereochemical aspects in the metabolism of the psychotomimetic amine 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane.** In: Abstracts of Papers, American Chemical Society (abstract MEDI 019). Chicago, 166th ACS National Meeting, August 26-31, 1973.

The fate of the psychotominmetic amine, 1-(2,5-dimethoxy-4-methylphenyl)- 2-aminopropane studied in connection with the role of the C-2 chiral center was reported in the 166th Meting of the American Chemical Society. In vivo and in vitro investigations were conducted. The absolute configurations were found to be S-(+) and R-(-). Racemic 1 was administered to rabbits and the urine was examined for unchanged compound ratio. Incubation of racemic 1 in rabbit liver homogenates resulted in almost exclusive metabolism of the S-isomer. When the individual isomers were incubated separately in rabbit liver homogenates, however, the S-isomer proved to be the better substrate. The identification and stereochemistry of the metabolites was discussed. (Journal abstract modified)

175859 Century, Bernard. Mendel Research Laboratory, Elgin State Hospital, 750 S. State St., Elgin, IL 60120 **A role of the dietary lipid in the ability of phenobarbital to stimulate drug detoxification.** Journal of Pharmacology and Experimental Therapeutics. 185(2):185-194, 1973.

The ability of phenobarbital to stimulate drug metabolism by liver was evaluated in Sprague-Dawley rats fed semisynthetic diets containing lipids which varied in their fatty acid compositions. Highest stimulation of drug metabolism was observed in phenobarbital pretreated animals fed linseed or menhaden oils. The least induction is found in animals fed either beef fat or low levels of corn oil. The ability of phenobarbital to increase rates of recovery from hexobarbital was highest in rats fed linseed and menhaden oils. Diet related differences in recovery from hexobarbital treatment is seen in both phenobarbital and saline pretreated mice but not in saline pretreated rats. These studies call attention to the dietary lipid as a pharmacological tool for varying cellular functions and drug responses, as well as a means of varying acid compositions in tissue components. 30 references. (Author abstract modified)

175895 Belknap, J. K.; Waddingham, Stephanie; Ondrusek, Gene. University of Texas, Austin, TX 78712 **Barbiturate dependence in mice induced by a simple short-term oral procedure.** Physiological Psychology. 1(4):394-396, 1973.

A procedure (adulterated millet diet) for inducing phenobarbital dependence in mice is presented. Marked withdrawal symptoms, including convulsions, were readily produced. In comparison with C57BL/6J mice, DBA/2J mice showed markedly greater intoxication and withdrawal, while consuming less phenobarbital during the same period. Thus, DBA/2J animals showed a heightened sensitivity to phenobarbital dependence than did C57BL/6J animals. 14 references. (Journal abstract modified)

176307 Hornbuckle, Phyllis A.; Collings, Virginia B. Virginia Commonwealth University, Richmond, VA **Drug effects on gastric ulceration rate in the rat. (Unpublished paper).** Final Report, NIMH Grant 19108, 1973. 11 p.

The effect of systematic manipulation of variables believed to influence levels of neural activity on restraint produced ulceration in the rat was investigated. A significant caudate lesion effect was found but both the noise and the noise by lesion interaction were not significant. Experiment B involved the effect of two drugs thought to act on neurological levels of activity, amphetamine sulfate and sodium pentobarbital, on ulceration rate. Both drugs were found to significantly depress ulceration development when compared with a saline control group, except for the highest levels of amphetamine. With a 3 hour restraint plus cold condition, and using D-amphetamine instead of amphetamine sulfate, a significant decrease in ulceration was noted at 0.05mg/kg whereas 9.0mg/kg produced a significant facilitation of ulceration. Intermediate dose level effects did not differ significantly from the saline control group. 12 references.

176312 Martin, William R.; Eades, Charles G.; Thompson, James A.; Gilbert, Paul E.; Sandquist, Virginia L.; Workman, Morgan. NIMH, Addiction Research Center, Lexington, KY **Progress report on the use of the dog for assessing morphine-like and nalorphine-like agonists as well as depot preparations of antagonists. (Unpublished paper).** Lexington, KY, NIMH, 1974, 12 p.

The use of the dog for assessing morphine like and nalorphine like agonists as well as depot preparations of antagonists was discussed. Pentazocine depresses the flexor reflex evoked by all three strengths of stimuli and is approximately one third as potent as morphine. The skin twitch is depressed by pentazocine. Morphine decreases pulse rate, lowers body temperature, constricts pupils, and stimulates respiration to a much greater extent than pentazocine. 1-BC-2605 has a significant agonistic activity but is approximately one fourth as potent as cyclazocine. M-5050 has agonistic actions in depressing the flexor reflex. It is around 8-10 times as potent as morphine in depressing the flexor reflex, but a ceiling effect was clearly evident at all stengths of stimuli. 4 references.

176677 Plotnikoff, Nicholas P.; O'Brien, George S. Dept. of Pharmacodynamics, Abbott Laboratories, North Chicago, IL 60064 **Comparison of anticonvulsant effects of clorazepate dipotassium and diazepam: four week anticonvulsant study in Rhesus monkeys.** Diseases of the Nervous System. 35(2):87-90, 1974.

The anticonvulsant effects of clorazepate dipotassium and diazepam were compared using Rhesus monkeys. Clorazepate dipotassium and diazepam were administered daily for the first 5 days of each week to the monkeys at equimolar

doses and challenged once a week with a convulsant dose of pentylenetetrazol. Clorazepate exhibited sustained anticonvulsant activity throughout the second, third, and fourth weeks while diazepam was effective only during the second and third weeks. 7 references.

176703 Leterrier, Francois R.; Rieger, Francois; Mariaud, Jean-Francois. Centre de Recherches du Service de Sante des Armees, 1 bis rue du Lt. R. Batany, 92140 Clamart, France **Comparative studies of synaptic membrane protein solubilization by chlorpromazine and sodium dodecylsulfate.** Biochemical Pharmacology (Oxford). 23(2):103-113, 1974.

The effects of chlorpromazine (CPZ) and of a true detergent sodium dodecylsulfate (SDS) on the spin labelled rat brain synaptic membrane is described. Biochemical and biophysical properties of CPZ are enumerated in detail. Protein yield for various concentrations and ESR spectra were measured in rat spin label membranes for immobilization properties. Brain membrane spectra changes for both compounds proved similar. SDC solubilizing action can be observed with concentrations much lower than generally used. Significant differences in properties of both compounds were noted. SDS acts on the whole depth of membrane structure. The mild detergent like action of CPZ is tentatively correlated with some biochemical properties of phenothiazine drugs. Polyacrylamide gel electrophoresis and sucrose gradient centrifugation were also conducted. 36 references.

176746 Kuschinsky, K. Abteilung Biochemische Pharmakologie, Max-Planck-Institut fur experimentelle Medizin, Hermann-Rein-Strasse 3, D-34 Gottingen, West Germany **Evidence that morphine increases dopamine utilization in corpora striata of rats.** Experientia (Basel). 29(11):1365-1366, 1973.

Striatal dopamine (DA) turnover as a result of morphine dosage was investigated in rats using a previously tested approach, in which alpha-methly-p-tyrosine was used to blackade catecholamine synthesis. Data reveal that morphine, unlike the neuroleptics, does not block DA neural receptors. It is still a matter of question as to whether or not the impulse flow, in contrast to the DA utilization, in stiratal dopaminergic neurons is in fact increased. The primary site of action of morphine seems to be a presynaptic one and might be some kind of diversion of newly synthesized DA from storage sites to sites of catabolism, leading to a lack of amine at the receptor sites, and resulting in a central DA deficiency syndrome with symptoms such as hypokinesia, catelepsy, and muscular rigidity. 11 references. (Author abstract modified)

176747 Perez-Reyes, M.; Timmons, Martha C.; Davis, K. H.; Wall, E. M. Department of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, NC 27514 **A comparison of the pharmacological activity in man of intravenously administered delta9-tetrahydrocannabinol, cannabinol, and cannabidiol.** Experientia (Basel). 29(11):1368-1369, 1973.

The pharmacological activities and relative potencies of delta9-tetrahydrocannabinol (delta9-THC), cannabinol, and cannabidiol were investigated in human Ss. Ss varied in their previous experience with marihuana and rated themselves subjectively on drug effects at appropriate intervals for 6 hr following drug administration. The initial perception of drug effect occurred with a small amount of delta 9-THC, a large amount for cannabinol, and cannabidiol did not produce a noticeable effect. The total dose of delta9-THC tolerated by Ss was relatively small and produced intense psychological and physiological effects. The total dose of cannabinol infused was large, on the other hand, and Ss never asked for it be terminated. After the experiment Ss repeated that they had been 'higher' previously with either marihuana or hashish smoking and that the experiment had been pleasant. Contrary to results obtained with the Rhesus monkey, it was found that cannibinol is capable of producing a marihuana like 'high' although the doses necessary for it are several orders of magnitude larger than those of delta9-THC. Findings indicate the need for caution in extrapolating results obtained in animal experimentation to man. (Author abstract modified)

176870 Lahti, Robert A.; Losey, E. G. CNS Diseases Research, Upjohn Co., Kalamazoo, MI 49001 **Antagonism of the effects of chlorpromazine and morphine on dopamine metabolism by GABA.** Research Communications in Chemical Pathology and Pharmacology. 7(1):31-40, 1974.

Possible GABA effects on the nigro-striatal dopaminergic system were studied. GABA levels were elevated by use of amino-oxyacetic acid, an inhibitor of GABA metabolism. Drugs were injected intraperitoneally into rats and dopamine was determined. Results indicated that elevated

levels of GABA, brought about by pretreatment with AOAA, will antagonize the effects of chlorpromazine and morphine on dopamine turnover in the rat striatum. Amino-oxyacetic acid pretreatment also blocked the homovanillic acid elevating property of chlorpromazine, but had no effect on dopamine decline after alpha-methyl-p-tyrosine treatment. The effect of GABA is observed only during blockade of dopamine receptors and is not observed under normal or receptor stimulated conditions. 18 references. (Journal abstract modified)

176874 Chiueh, C. C.; Moore, K. E. Department of Pharmacology, Michigan State Univ., East Lansing, MI 48824 **Relative potencies of d- and l-amphetamine on the release of dopamine from cat brain in vivo.** Research Communications in Chemical Pathology and Pharmacology. 7(1):189-199, 1974.

Amphetamine-induced relases of dopamine and/or norepinephrine from brain demonstrated in vivo. Cats were anesthetized with sodium pentobarbital and prepared for ventricular perfusion. After the administration of 3H-dopamine, the cerebro ventricular system of anesthetized cats was perfused with artificial cerebrospinal fluid (CSF). The addition of dextro or l-amphetamine to the perfusing CSF produced a dose-related increase in the efflux of 3H-dopamine from the cat brain; d-amphetamine was approximately ten times more potent and three times more effective than l-amphetamine. These test effects may be related to the relative abilities of these two isomers of amphetamine to influence the dynamics of dopamine in the striatum. 21 references. (Journal abstract modified)

176880 Abel, E. L. Research Institute on Alcoholism, New York State Dept. of Mental Hygiene, 1021 Main St., Buffalo, NY 14203 **Chronopharmacology of delta9-tetrahydrocannabinol hypothermia in mice.** Experientia (Basel). 29(12):1528-1529, 1973.

A study to determine whether the thermogenic effects of delta9-tetrahydrocannabinol (Delta-THC) on mice would be affected by the chronological time of injection was made. The time of day at which injections were made was found to constitute a significant variable in determining the magnitude of drug effect. The greater degree of effect appeared when animals were injected in the afternoon and the smallest change in body temperature occured when injections were administered at night. Results are discussed in terms of animal activity. 5 references.

176881 Singh, G. B.; Nityanand, Swaran; Srimal, R. C.; Rao, V. A.; Jain, P. C.; Dhawan, B. N. Central Drug Research Institute, Chattar Manzil Palace, Lucknow-1, India **Antihypertensive and central nervous system depressant properties of 3-(gamma-p-fluorobenzoyl propyl) 2, 3, 4, 4a, 5, 6-hexahydro-1(H)-pyrazino (1,2-a) quinoline hydrochloride (compound 69-183, centpyraquin.** Experientia (Basel). 29(12):1529-1530, 1973.

The antihypertensive and central nervous system (CNS) depressant properties of centpyraquin, 3-(gamma-p-flurobenzoyl propyl) 2,3,4,4a5, 6-hexahydro-1(H)-pyrazino (1,2-a) quinoline hydrochloride are reported. The following results are discussed: cardiovascular and automic effects in normotensive cats and dogs; effect in hypertensive rats; CNS effects in mice; blockade of conditioned avoidance and unconditioned response in rats; and the behavioral effects in monkeys and cats. It was concluded that centpyraquin posesses potent hypotensive and CNS depressant properties. The site of the hypotensive action appears to be peripheral, possible at adrenergic neurones, since the compound blocks the contraction of the nictitating membrane due to preganglionic as well as postganglionic sympathetic nerve stimulation and tyramine pressor response, while adrenaline and noradrenaline pressor responses are potentiated. The CNS properties resemble those of a major tranquillizer. 4 references. (Author abstract modified).

176936 Sharpless, Nansie S.; Tyce, Gertrude M.; Owen, Charles A., Jr. Mayo Clinic and Mayo Foundation, Rochester, MN **Effect of chronic administration of L-dopa on catechol-O-methyltransferase in rat tissues.** Life Sciences (Oxford). 12(3):97-106, 1973.

The activity of catechol-O-methyltransferase (COMT) in rat brain and peripheral tissues was studied during prolonged oral administration of L-dopa. COMT activity was stable in most tissues of rats fed a diet containing 1% L-dopa for 52 weeks. Small decreases in activity, which cannot be explained by either the age of the rats or the presence of inhibitory substances, slowly appeared only in liver and kidney. Activity in erythroctyes, which was 10 times greater in rats than in humans when optimal assay conditions were used, was unaffected by L-dopa treatment. The lack of adaptive increases in COMT may ex-

plain, in part, the observed lack of 'fall-off' in the therapeutic efficacy of L-dopa. 18 references. (Author abstract)

177021 Chand, N.; Gupta, M. L.; Gupta, T. K.; Bhargava, K. P. Department of Pharmacology and Therapeutics, King George's Medical College, Lucknow-3, India **A study of anti-ovulatory activity of haloperidol in rabbits.** Japanese Journal of Pharmacology (Kyoto). 23(6):827-829, 1973.

The effect of haloperidol was studied on the ovulation induced by progesterone, copper acetate, and coitus in adult female rabbits. Progesterone induced ovulation was blocked by prior treatment with haloperidol, but it was found to have no effect on copper acetate induced ovulation. Treatment of rabbits with haloperidol before coitus resulted in loss of receptivity in all the rabbits tested. The results indicate that central adrenergic or dopaminergic mechanisms are involved in progesterone induced ovulation and copper acetate may be acting directly at median eminence to bring about the release of LHRF. The precoital administration of haloperidol in female rabbits resulted in loss of receptivity. 14 references. (Journal abstract)

177022 Shimizu, Kazunori. Second Division of Department of Pharmacology, Showa University, Shinagawa-ku, Tokyo, Japan **Studies on monoamine oxidase -- Report 22: Effects of NaNO2 and NH2OH on mitochondrial MAO in rat brain.** Japanese Journal of Pharmacology (Kyoto). 23(6):831-838, 1973.

The effects of sodium nitrite and hydroxylamine on mitochondrial monoamine oxidase (MAO) from rat brain were studied with the following results: sodium nitrite and hydroxylamine activated the enxyme, but the effects on enzyme activity differed with different substrates. The activating effects were reversible. Sodium nitrite did not cause activation at any concentration of pheniprazine and pargyline tested. Different quantities of hydroxylamine decreased the inhibitions by pheniprazine and pargyline at all concentrations of the inhibitors tested. 12 references. (Journal abstract)

177128 Holz, R. W.; Deguchi, T.; Axelrod, J. Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, MD 20014 **Stimulation of serotonin N-acetyltransferase in pineal organ culture by drugs.** Journal of Neurochemistry (Oxford). 22(2):205-209, 1974.

Drugs such as cocaine, procaine, pheniprazine and veratridine were examined for their ability to increase serotonin N-acetyltransferase (NAT) in pineal organ culture. The absence of potassium was also examined. NAT is known to respond to beta adrenergic stimulation. Results indicate that these agents activated the beta adrenergic receptor on pineal cells by causing an accumulation of extraneuronal norepinephrine. This accumulation is due, at least in part, to the blockage of norepinephrine reuptake by nerve terminals. The ability of veratridine to stimulate NAT and to inhibit norepinephrine uptake was reversed by tetrodotoxin, a blocker of sodium permeability in excitable tissue; thus veratridine acts by increasing sodium permeability in nerve terminals. 20 references. (Author abstract modified)

177131 Horn, A. S.; Cuello, A. C.; Miller, R. J. Department of Pharmacology, University of Cambridge Medical School, Cambridge, England **Dopamine in the mesolimbic system of the rat brain: endogenous levels and the effects of drugs on the uptake mechanism and stimulation of adenylate cyclase activity.** Journal of Neurochemistry (Oxford). 22(2):265-270, 1974.

Two areas of the mesolimbic dopamine system were studied for the presence of a benztropine sensitive dopamine uptake system and the existence of dopamine sensitive adenylate cyclase activity. High concentrations of dopamine were found in the nucleus accumbens and olfactory tubercle using a radiochemical enzymatic assay technique. An active uptake system for (3H)dopamine that is temperature sensitive and dependent on external sodium ions is present in synaptosome rich homogenates of these two brain areas. This uptake process is potently inhibited by benztropine. Dextroamphetamine d was 4.5times more potent than l-amphetamine in inhibiting dopamine uptake in the nucleus accumbens and six times more potent in the olfactory tubercle and corpus striatum. Low concentrations of dopamine caused an increase in adenosine 3'5'-monophosphate (cyclic AMP) formation in both areas. This effect was potently blocked by chlorpromazine. The alpha adrenoceptor antagonist phentolamine weakly antagonized the stimulation of this adenylate cyclase by dopamine, but the beta adrenoceptor antagnoist propranolol did not. 35 references. (Author abstract)

177135 King, Lucy J.; Carl, Juanita L.; Lao, Lauro. Dept. of Psychiatry, School of Medicine,

Washington University, St. Louis, MO 63110 **Brain amino acids during convulsions.** Journal of Neurochemistry (Oxford). 22(2):307-309, 1974.

Brain levels of selected amino acids were compared in mice after electroshock. One group of mice was pretreated with phenobarbitone and a control group was untreated with the drug. Glutamate did not change significantly during convulsions. Both glutamine and GABA were significantly higher mice that did not receive phenobarbitone. Aspartate and alanine did not change significantly in either group of mice but aspartate in phenobarbitone treated mice was significantly higher than in 'no drug' mice. Ammonia did not change during the first 3 seconds after stimulation of no drug mice, but it then rose rapidly and remained elevated through 50 seconds. Ammonia concentration in no drug mice was significantly higher than in phenobarbitone treated animals. 8 references.

177252 Skolnick, Phil; Daly, John W. National Institute of Arthritis, Metabolism and Digestive Diseases, Bethesda, MD 20014 **Norepinephrine-sensitive adenylate cyclases in rat brain: relation to behavior and tyrosine hydroxylase.** Science. 184(4133):175-177, 1974.

Magnitudes of spontaneous motor and tyrosine activities and AMP in rat midbrains were investigated. Responses of norepinephrine sensitive adenosine 3', 5'-monophosphate (cyclic AMP)-generating systems in combined midbrain - striatal slices of four rat strains correlate positively with spontaneous behavioral activity and negatively with levels of midbrain and straital tyrosine hydroxylase. Responses of cerebral cortical norepinephrine sensitive cycle AMP systems correlate negatively with spontaneous behavioral activity and positively with midbrain and striatal tyrosine generating systems to isoproterenol, adenosine, veratridine, or of an adenosine and norepinephrine combination. 19 references. (Journal abstract modified)

177332 Roth, Jerome A.; Gillis, C. N. Departments of Anesthesiology and Pharmacology, Yale University School of Medicine, New Haven, CT 06510 **Inhibition of lung, liver and brain monoamine oxidase by imipramine and desipramine.** Biochemical Pharmacology (Oxford). 23(6):1138-1140, 1974.

Evidence is presented which suggests that tricyclic antidepressant drugs, imipramine and desipramine, are effective inhibitors of monoamine oxidase (MAO) in vitro in the lung, liver and brain of the rabbit. The data shows the ability of the tricyclic antidepressant drugs to inhibit deamination of 5-hydroxytryptamine, norepinephrine and other biogenic monoamines in vitro. The fact that desipramine also decreases metabolism of the secondary amine, epinephrine, establishes that these antidepressant drugs inhibit the enzyme MAO. 16 references.

177333 Gill, Edward W.; Lawrence, David K. University Department of Pharmacology, South Parks Road, Oxford, England **Blood and brain levels of delta1-tetrahydrocannabinol in mice -- the effect of 7-hydroxy-delta1-tetrahydrocannabinol.** Biochemical Pharmacology (Oxford). 23(6):1140-1143, 1974.

The origin of a mixture of delta1-THC and cannabinol in the blood and brain extract of mice after injection of 3H-7-hydroxy-delta1-tetrahydrocannabinol (3H-7-hydroxy-delta1-THC) was investigated and the major component was identified by combined gas - liquid chromatography and mass spectroscopy (GLC-MS). The elevation of the brain concentration of both active cannabinoids (delta1-THC and 7-hydroxy-delta1-THC) at doses within the normal effective range suggests that if a nonpsychoactive drug with similar tissue binding characteristics were administered together with delta1-THC, the effect of the latter might be potentiated. Such a situation might arise in the context of multiple drug abuse. 6 references.

177334 Maickel, Roger P.; Harrison, Steadman D., Jr. Medical Sciences Program, Indiana University, Bloomington, IN 47401 **Inability of rat brain homogenate to oxidize amphetamine.** Biochemical Pharmacology (Oxford). 23(6):1146-1147, 1974.

Attempts to measure the production of metabolites of (3H)amphetamine by the rat brain dehydrogenase system as described by Guha and Mitra in various articles are reported. Contrary to their findings, no metabolic conversion of amphetamine was observed. 8 references.

177336 Niwaguchi, Tetsukichi; Inoue, Takako; Nakahara, Yuji. National Research Institute of Police Science, First Chemistry Section, Tokyo, Japan **Studies on enzymatic dealkylation of D-lysergic acid diethylamide (LSD).** Biochemical Pharmacology (Oxford). 23(6):1073-1078, 1974.

New dealkylated metabolites, D-lysergic acid monoethylamide (LAE) and D-N6-demethyl-lysergic acid diethylamide (nor-LSD), were formed by incubation of D-lysergic acid diethylamide (LSD) with rat liver 9000 g supernatant fractions. It was elucidated that these dealkylations were mediated by an NADPH and oxygen dependent enzyme in liver microsomes and were inhibited by SKF 525-A. Tranquilizing agents, such as chlorpromazine, nitrazepam and meprobamate, and certain brain monoamines, inhibited these enzymatic dealkylations of LSD. Species differences were investigated. 23 references. (Author abstract)

177337 Rommelspacher, Hans; Honecker, Henning; Schulze, Gert; Strauss, Sabine M. Johns Hopkins University School of Medicine, Dept. of Pharmacology and Experimental Therapeutics, Baltimore, MD 21205 **The hydroxylation of D-amphetamine by liver microsomes of the male rat.** Biochemical Pharmacology (Oxford). 23(6):1065-1071, 1974.

The conditions under which the hydroxylation of amphetamine to p-hydroxyamphetamine can be studied in isolated rat liver microsomes are described. The reaction depends on the concentration of NADP. The optimal pH is 6-9 - 7-0. As Michaelis parameters 1-5 x 10-4M(Km) and 2-16 nmoles (mg of microsomal protein)-1 (10 min)-1 (Vmax) were calculated. The production of p-hydroxyamphetamine is not restricted to the microsomes but a smaller biotransformation of amphetamine was also found in mitochondria. 20 references. (Author abstract)

177338 Liuzzi, Antonia; Foppen, F. H.; Angeletti, P. U. National Institute of Mental Health, Laboratory of Clinical Science, Bethesda, MD 20014 **Adrenaline, noradrenaline and dopamine levels in brain and heart after administration of 6-hydroxydopamine and guanethedine to newborn mice.** Biochemical Pharmacology (Oxford). 23(6):1041-1044, 1974.

The adrenaline, noradrenaline and dopamine levels of the whole brain and heart of mice were measured spectrofluorimetrically after subcutaneous injection at birth with 6-hydroxydopamine or guanethedine. 6-Hydroxydopamine decreased noradrenaline and dopamine levels in brain tissue within 15 days after administration. Dopamine recovered within 45 days to an almost normal level. Both noradrenaline and dopamine decreased initially after guanethedine treatment, but differences from control values were insignificant 7 months after treatment. Dopamine and noradrenaline levels in heart decreased after both 6-hydroxydopamine and guanethedine treatment. The effect on adrenaline levels in brain and heart was statistically insignificant. It is suggested that 6-hydroxydopamine and guanethedine may cause long lasting lesions in some catecholamine containing neurons in the central nervous system. 11 references. (Author abstract)

177406 Antonaccio, M. J.; Smith, C. B. Department of Pharmacology, University of Michigan Medical School, Ann Arbor, MI 48104 **Effects of chronic pretreatment with small doses of reserpine upon adrenergic nerve function.** Journal of Pharmacology and Experimental Therapeutics. 188(3):654-667, 1974.

Effects of accelerans nerve stimulation on heartrate in open chest guinea pigs and of field stimulation upon force of contraction of isolated left atrial strips were determined after pretreatment with reserpine for 7 days. Dose response relationships were determined for norepinephrine and tyramine upon rate of beating of right atria and upon force of contraction of isolated left atrial strips. Reserpine decreased norepinephrine content and retention of 3H-norepinephrine in cardiac tissues. Right atria showed a three fold increase in sensitivity to norepinephrine after chronic reserpine treatment, whereas isolated left atrial strips showed no change in sensitivity. After reserpine, right atrial norepinephrine levels were reduced by 85%, but the frequency-response curves to accelerans nerve stimulation were shifted to the left. There were decreases in the maximum responses to field stimulation and to tyramine at these doses of reserpine. After reserpine treatment for 7 days, left atrial norepinephrine content was reduced by 91%. Although maximum responses to tyramine were also decreased, there were no changes in the frequency-response curves for either accelerans nerve stimulation or field stimulation. Results suggest that the store of norepinephrine necessary for the normal function of adrenergic neurons during nerve stimulation is extremely small. 35 references. (Author abstract)

177731 Alvin, John; Bush, Milton T. Department of Pharmacology, Vanderbilt School of Medicine, Nashville, TN 37232 **The metabolic fate of N,N'-dimethoxymethyl-phenobarbital in the rat.** Journal of Pharmacology and Experimental Therapeutics. 188(1):8-14, 1974.

The metabolic fate of N,N'-dimethoxymethylphenobarbital (DMMP) was studied in the rat. Approximately 90% of the radioactivity in a dose of DMMP-14C is excreted in the urine during 96 hours after administration. By complementary countercurrent distribution and thin layer chromatography procedures, the major labeled products were separated, identified and quantitated. Phenobarbital accounted for 5 to 13% of the dose, free p-hydroxyphenobarbital 41 to 49%, and conjugates of the latter 24 to 33%. Very small amounts of what is believed to be a conjugated hydroxy derivative of monomethoxymethylphenobarbital (MMP) were separated from the urine, but no DMMP. The second N-alkyl moiety was removed much more slowly than the first (4% in one hour) and the phenobarbital which was produced accounted for practically all of the MMP which disappeared. Even though significant amounts of MMP are not excreted, it is clear that this compound should be important in the pharmacological actions of DMMP. 12 references. (Author abstract modified)

177732 Holcomb, Robert R.; Gerber, Nicholas; Bush, Milton T. Dept. of Pharmacology, Vanderbilt Univ. School of Medicine, Nashville, TN **The metabolic fate of hexobarbital in the rat.** Journal of Pharmacology and Experimental Therapeutics. 188(1):15-26, 1974.

With the aid of 2-14C-hexobarabital (HB), the major metabolites of this drug in the rat were identified and quantitated, in vivo and in vitro. In the urine HB, 3-keto-HB and 3-hydroxy-HB (HO-HB) were mostly excreted during the first 12 hours after an i.v. dose. Only 4% of the 14C was excreted in the feces. The fortified 9000 x g supernatant fraction of liver homogenate metabolized HB almost exclusively to HO-HB in preparations from both normal and phenobarbital pretreated animals. In the isolated perfused liver system HO-HB accounted for most of the HB metabolized during the first 60 minutes, but keto-HB was the major metabolite after 90 minutes. By whole body analyses, it was shown that half of the dose was metabolized in 12 minutes. This time was increased to 81 and 90 minutes in two animals pretreated with SKF 525A. Since whole body analyses show t/2=12 minute, it was conclude that HB is metabolized in the rat at a rate much higher than previous reports have indicated. 32 references. (Author abstract modified)

177733 Randall, Carrie L.; Lester, David. Center of Alcohol Studies, Rutgers University, New Brunswick, NJ 08903 **Differential effects of ethanol and pentobarbital on sleep time in C57BL and BALB mice.** Journal of Pharmacology and Experimental Therapeutics. 188(1):27-33, 1974.

The lesser central nervous system sensitivity of C57BL as compared to BALB mice measured by the length of sleep induced by 4.0g/kg of ethanol was confirmed. Since C57BL mice prefer and BALB mice avoid drinking an alcohol solution in a choice situation, one aspect of the relation between the lesser central nervous system responsivity and the alcohol drinking was studied by a determination of the alcohol specificity of the central nervous system effect. Sleep induced by pentobarbital was of equal duration in these strains. Inasmuch as C57BL mice metabolized pentobarbital more rapidly and awakened at a lower level of brain and blood pentobarbital, it was concluded that C57BL mice had a greater sensitivity to pentobarbital than to ethanol, the reverse being true for the BALB mice. The hypnotic effect of ethanol is thus not generalizable and the results support the notion that different brain sites are involved and suggest that alcohol preference of various strains of mice may indeed be related to the central responsivity to alcohol. 32 references. (Author abstract)

177734 Cheng, H. C.; Long, J. P.; Nichols, D. E.; Barfknecht, C. F. Department of Pharmacology, College of Medicine, University of Iowa, Iowa City, IA 52242 **Effects of psychotomimetics on vascular strips: studies of methoxylated amphetamines and optical isomers of 2,5-dimethoxy-4-methylamphetamine and 2,5-dimethoxy-4-bromoamphetamine.** Journal of Pharmacology and Experimental Therapeutics. 188(1):114-123, 1974.

Superfused vascular strips of dog dorsal metatarsal vein were used to study effects of methoxylated amphetamines and the optical isomers of 2,5-dimethoxy-4-methylamphetamine (DOM) and 2,5-dimethoxy-4-bromoamphetamine (DOB) on sympathetic nervous systems and on 5-hydroxytryptamine (5-HT) receptors. All these amphetamine derivatives produced long lasting contractions of the superfused strips. Contractions induced by para-methoxyamphetamine (PMA), 2,4-dimethoxyamphetamine (DMA), 2,5-DMA, 3,4-DMA and (+)-DOM were reduced by phentolamine whereas contractions produced by (-)-DOM, (dl) DOB, (+) DOB and (-)-DOB were not reduced. Contractions elicited by PMA, 2,4-

DMA and 3,4-DMA were antagonized by cocaine but those produced by 2,5-DMA, (+)-DOM and (-)-DOM; (dl)-DOB, (+)-DOB and (-)-DOB were not antagonized. Responses of the vascular strips to (+)-DOM and (-)-DOM; (dl)-DOB, (+)-DOB and (-)-DOB were greatly antagonized by cinanserin, a 5-HT receptor antagonist. It was concluded that PMA, 2,4-DMA and 3,4-DMA produced contractions by releasing norepinephrine from sympathetic nerve terminals whereas 2,5-DMA elicited muscle contractions by directly stimulating alpha adrenergic receptors and that (+)-and (-)-DOM; (dl)-DOB, (+)-DOB and (-)-DOB activate 5-HT receptors. PMA is the most potent in this series of compounds. The S-(+) isomers of both DOM and DOB are more potent than their corresponding R-(-) isomers in activating 5-HT receptors. 37 references. (Author abstract)

177749 Guerrero-Figueroa, R.; Guerrero-Figueroa, E.; Sneed, G. A.; Kennedy, M. J. Southeast Louisiana Hospital, Mandeville, LA **Effects of lorazepam on CNS structures: neurophysiological and behavioral correlations.** Current Therapeutic Research. 16(2):137-146, 1974.

Local evoked potentials (LEP), multiple unit activity, and gross behavior were studied in unrestrained, unanesthetized normal and epileptic cats and monkeys during single and chronic administration of lorazepam. The compund administered by parenteral route produced a strong inhibitory action upon the epileptiform activity recorded from secondary subcortical and cortical epileptogenic tissues in association with a weak inhibitory action upon the epileptiform activity generated from primary subcortical epileptogenic foci. Oral administration of lorazepam possesses a weak inhibitory effect upon epileptiform activity recorded from secondary subcortical and cortical epileptogenic tissues and no effects upon the electrical activity recorded from primary cortical or subcortical epileptogenic foci. 22 references. (Author abstract modified)

177835 Breitbart, H.; Perl, M.; Mayevsky, A.; Diamant, E. Y. Department of Life Sciences, Bar Ilan University, Ramat Gan, Israel **Brain ribosomal RNA synthesis inhibited by chlorpromazine.** Proceedings of the Society for Experimental Biology and Medicine. 143(1):204-207, 1973.

The effect of cholorpromazine (CPZ) on in vivo RNA synthesis in the rat brain was investigated. Such injections cause a depletion in 3H-uridine incorporation in the brain ribosomal RNA. This phenomenon occurs in both 18s and 28s fractions. An effect on transcription may explain the reported influences of the drug on brain metabolism, particularly on ATPase activity. 14 references. (Author abstract modified)

177840 Thornburg, J. E.; Moore, K. E. Department of Pharmacology, Michigan State University, East Lansing, MI 48823 **Inhibition of anticholinergic drug-induced locomotor stimulation in mice by alpha-methyltyrosine.** Neuropharmacology (Oxford). 12(12):1179-1185, 1973.

The inhibition of anticholinergic drug induced locomotor stimulation by alpha-methyltyrosine was studied in mice in an attempt to distinguish between an anticholinergic or a dopaminergic mechanism of action for such stimulating activity. Alpha-Methyltyrosine, administered in the diet, inhibited locomotor stimulation induced by benzotropine, scopolamine, and atropine. FLA-63, administered similarly, did not alter any of the drug stimulated activities. Results suggest that a dopaminergic system is involved in the pathway mediating anticholinergic drug induced locomotor stimulation. 28 references. (Author abstract)

177976 Barker, J. L.; Nicoll, R. A.; Padjen, A. National Institute of Child Health and Human Development, Bethesda, MD 20014 **Action of convulsants on root potentials and amino acid responses in isolated frog spinal cord. (Unpublished paper).** Washington, DC, NIMH, 1974. 40 p.

In the isolated frog spinal cord, picrotoxin, bicuculline, and strychnine were evaluated for their effects on depolarizations of primary afferents that were induced synaptically or by amino acids. Results suggest that there are at least three distinct populations of neutral amino acid receptors on primary afferent terminals: a gamma-aminobutyric acid (GABA) like receptor, a taurine/beta-alanine receptor, and a glycine like receptor. The strychnine resistance of the glycine responses indicates that the primary afferent receptors for glycine differ from those on the somata of spinal neurons. The results further suggest that: 1) a GABA like transmitter mediates the final step in the dorsal root - dorsal root potential and lateral column - dorsal root potential pathways; and 2) either taurine or beta-alanine may mediate the last step in the ventral root - dorsal root potential pathway. 58 references. (Author abstract modified)

178557 Spilker, B. A.; Dhasmana, K. M. Dept. of Pharmacology, Sterling-Winthrop Research Institute, Rensselaer, NY 12144 **On the specificity of dopamine release by amantadine.** Experientia (Basel). 30(1):64-65, 1974.

A study to determine whether amantadine could be shown to release norepinephrine (NE) in dogs under in vivo conditions was reported. Amantadine caused a greater blood pressure rise in dogs loaded with dopamine than with saline, a fact which suggests that Amantadine caused a release of dopamine. This effect was not due to a general release of catecholamines, since no differences from controls were observed after loading the animal with NE. The increased rise in blood pressure to each subsequent dose of NE but not dopamine confirms other reports that Amantadine blocks the uptake of NE and suggests that it does not block the uptake of dopamine. 6 references. (Author abstract modified)

178558 Brus, R.; Herman, Z. S.; Sokola, A.; Jamrozik, Z. Dept. of Pharmacology, Institute of Biology and Physiology, Silesian School of Medicine, PL-41-808 Zabrze, Poland **Effect of 6-hydroxydopamine on the duration of hexobarbital sleep in rats.** Experientia (Basel). 30(1):66, 1974.

The duration of hexobarbital sleep in rats after chemical sympathectomy of the central nervous system was studied. The marked prolongation of the time of hexobarbital sleep after an i.v. injection of 6-hydroxydopamine-hydrochloride was established in comparison to control groups. No differences were noted in the time of sleep of controls. Results confirm the role of catecholamines in hypnotic action of hexobarbital, but their role in the mechanism is complex and difficult to explain. 17 references. (Author abstract modified)

178640 Doggett, Neil S. Dept. of Applied Pharmacology, Welsh School of Pharmacy, UWIST, King Edward VII Avenue, Cardiff, Great Britain **Interaction of centrally-administered ouabain with agents affecting sympathetic function.** Life Sciences (Oxford). 12(3):121-129, 1973.

The extent to which a primary interference with the noradrenergic systems is responsible for ouabain induced hypothermia in the mouse is investigated. The interactions of ouabain with noradrenaline, phentolamine, alpha-methyl-metatyrosine and (plus)-amphetamine indicate that the hypothermia produced by small doses injected into the cerebral ventricles of the conscious mouse does not primarilly involve an interference with noradrenergic systems within the brain. However, a direct action on thermoregulation, including a multiple interference with amine function, is possible. 17 references. (Author abstract)

178641 Pittman, Kenneth A. Metabolic Chemistry Section, Sterling-Winthrop Research Institute, Rensselaer, NY **Pentazocine in rhesus monkey plasma and brain after parenteral and oral administration.** Life Sciences (Oxford). 12(3):131-143, 1973.

Data are presented to show that absorption of orally administered pentazocine is rapid in the monkey, and that a more rapid metabolism is the reason for the appearance of less pentazocine in the plasma after oral administration than after parenteral administration of the drug. Pairs of female rhesus monkeys were given either 0.5mg radioactive pentazocine/kg intramuscularly or 1.5mg orally and killed at intervals up to 2 hr. Plasma and cerebral tissue were analyzed for pentazocine and metabolites and other tissues for total radioactivity. Pentazocine was the only radioactive compound found in cerebral tissue from intramuscularly dosed Ss and was always an order of magnitude higher in concentration than was plasma pentazocine. Cerebral and plasma pentazocine concentrations in orally dosed Ss were one to two orders of magnitude lower than those in intramuscularly dosed Ss. It is concluded that pentazocine is metabolized by the monkey as rapidly as it is absorbed. 11 references. (Author abstract)

178720 Houser, Vincent P.; Pare, William P. Pavlovian Research Laboratory, Veterans Administration Hospital, Perry Point, MD 21902 **anticholinergics: their effects on fear-motivated behavior, urinary ll-hydroxycorticosteroids, urinary volume, and heart rate in the dog.** Psychological Reports. 34(1):183-197, 1974.

The effects of two anticholinergics (scopolamine hydrobromide and scopolamine methylbromide) on fear motivated behavior, urinary ll-hydroxycorticosteroids, urinary volume, and heartrate in the dog were investigated. Ss were given the drugs and subjected to a Sidman nondiscriminated avoidance schedule which contained seven conditioned stimuli - unavoidable shock (CS - US) pairings. Both drugs significantly elevated urinary ll-hydroxycorticosteroids and

heartrate, while only the centrally acting agent, scopolamine hydrobromide, affected behavior. Results suggest that the behavioral effects of this drug are not mediated through its effects on the adrenal-pituitary system. Response rates under scopolamine hydrobromide were substantially reduced, leading to increased shock rates, especially during the CS segments of the schedule. These behavioral results suggest that cognitive (possibly memory) functions were altered in response to scopolamine administration. 15 references. (Author abstract)

178725 Nakahara, Tanio; Hanabusa, Yasuhiko; Ushizima, Itsuko; Morishita, Hideji; Kazama, Kaoru; Ono, Nobufumi; Kushiku, Kazushi; Furukawa, Tatsuo. Department of Pharmacology, Fukuoka University, Fukuoka, Japan **Pharmacological studies on bromazepam.** Igaku Kenkyu (Fukuoka). 43(1):27-40, 1973.

The pharmacological effects of a new benzodiazepine derivative, bromazepam (7-bromo-5-(2-pyridyl)-3H-1,4-benzodiazepine-2(1H)-one), were studied and compared with those of diazepam and chlordiazepoxide. The results indicate that bromazepam has the strongest central action, followed by diazepam and chloridiazepoxide. With an effective dose of the central action, bromazepam has slight effects on the cardiovascular system and smooth muscle, and its LD50 is larger than that of diazepam and chlordiazeposide. 10 references. (Journal abstract modified)

178747 Thoa, Nguyen B.; Wooten, G. Frederick; Axelrod, J.; Kopin, I. J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Mechanism of release at noradrenergic nerve terminals by reserpine and several sympathomimetic agents. (Unpublished paper).** Bethesda, MD, NIMH, 1973, 24 p.

The mechanism of norepinephrine release induced by tyramine, d-amphetamine, metaraminol and reserpine was studied in the isolated guinea pig vas deferens. Experiments involved both the incubation of isolated guinea pig vasa deferentia in vitro in the presence of varying concentrations of reserpine, tyramine, d-amphetamine, or metaraminol, and in vivo pretreatment of guinea pigs with reserpine, and with a monoamine oxidase inhibitor in addition to reserpine. It is concluded that norepinephrine appears to be released at noradrenergic terminals by at least two distinct mechanisms: (1) depolarization induced release or exocytosis characterized by dependence on extracellular calcium, blocked by tetrodotoxin and colchicine, with released norepinephrine arising from the vesicular storage particles; and (2) sympathomimetic drug induced release not accompanied by release of vesicle specific proteins, independent of extracellular calcium ion, not blocked by colchicine or tetrodotoxin and arising from extravesicular cytoplasmic pools. 23 references. (Author abstract modified)

178812 Carper, W. R.; Stoddard, D. D.; Martin, D. F. Dept. of Chemistry, Wichita State University, Wichita, KS 67208 **Choline activation of lithium transport.** Experientia (Basel). 29(10):1249-1250, 1973.

Choline activation of lithium transport was studied in order to devise a system in which lithium transport would be accelerated to achieve therapeutic effects through lower dosage levels. Such a system is one in which choline facilitates the initial flow of lithium across bovine erythrocyte membranes. A preliminary report of the study is presented, the full details of which will be published elsewhere. Findings indicate that choline increases lithium's normal transfer rate for both influx and efflux. 19 references.

178814 Vernadakis, Antonia. Depts. of Pharmacology, University of Colorado School of Medicine, Denver, CO 80220 **Changes in brain acetylcholinesterase activity of young rats after chronic treatment with tremorine.** Experientia (Basel). 29(10):1257-1259, 1973

Changes in brain acetylcholinesterase (AChE) activity of young rats after chronic treatment with tremorine were studied. Subjects were Sprague-Dawley male rats, 60 days of age. Tremorine was administered to the rats daily for 7 days in doses of 7.5, 22.5, or 30mg/kg. Animals receiving the lowest dose exhibited only light jaw tremor, while the other two groups exhibited more intense patterns of convulsive movements. Four days after cessation of treatment, the animals were sacrificed, and the brains dissected. AChE activity was found to be markedly higher in the cerebral cortex of the animals which received the highest dose of tremorine. It is suggested that the high AChE activity in the cerebral cortex after tremorine may reflect a high turnover rate of acetylcholine ACh and thus may explain the lack of changes of ACh in this central nervous system structure. 8 references.

178815 Parvez, H.; Parvez, S. University of Paris, Centre of Orsay, Laboratory of Endocrinology, Bat.491, F-91 Orsay, France **The rate limiting control of enzymes monoamine oxidase and catechol-O-methyl transferase in the foetus and the adult by adreno-cortical hormones.** Experientia (Basel). 29(10):1259-1262, 1973

The rate limiting control of enzymes monoamine oxidase (MAO) and catechol-O-methyl transferase (COMT) in the fetus and the adult by adreno-cortical hormones was studied. Subjects were white New Zealand rabbits and Sherman rats. Female rabbits were made pregnant, and on the 20th day fetal hypophysectomy by decapitation was performed. Another group of fetuses from unoperated mothers served as controls. Decapitated fetuses were administered 1.5mg of hydrocortisone or 1.2IU of ACTH postoperatively. Newborn rats were adrenalectomized bilaterally under ether anesthesia just after birth. Tissues from normal and adrenalectomized young rats were excised 10 days after the operation. Adult male rats were administered 75mg of metopirone in olive oil ip. The tissues were dissected 8 hours after the metopirone injection. Findings indicate that glucocorticoids inhibit MAO and COMT activities both in vivo and in vitro. Clinical implications for the treatment of neuroleptic disorders are discussed. 34 references.

178945 Schumpelick, V. Physiologisches Institut der Universitat, 2000 Hamburg 20, Martinistr. 52, Germany **/The effect of diazepam on some cardiovascular and respiratory reflexes elicited by afferent abdominal vagus stimulation./** Wirkung von Diazepam auf einige durch afferente abdominale Vagusreizung ausgeloste kardiovaskulare und respiratorische Reflexe. Arzneimittel-Forschung (Aulendorf). 23(4):514-519, 1973.

In 45 urethan anesthetized male albino rats the effect of diazepam on cardiovascular and respiratory reflexes, elicited by afferent stimulation of the abdominal vagus was studied. Results included: 1) inhibition of the reflex bradycardia; 2) reduction of vagal arrhythmia; 3) 50% shortening of the initial apnea; and 4) 35% diminishing of the depressor and pressor components of blood pressure alteration. The diazepam effect was not dose dependent and related to reflex responses only, for, in contrast to atropine, bradycardia elicited by direct stimulation of the peripheral cut end of the cervical vagus was not inhibited by diazepam. A central action of this compound on the autonomic reflex centers in the limbic system and the hypothalamus is discussed. 35 references.

178947 Gogolak, G.; Stumpf, Ch.; Tschakaloff, Ch. Lehrkanzel fur Neuropharmakologie der Universitat, A-1090 Wien, Wahringerstr. 13a, Austria **/Anticonvulsant activity of clonazepam and Ro 8-4192 against penicillin and lidocaine induced seizures./** Antikonvulsive Wirkung von Clonazepam und Ro 8-4192 gegen Penicillin- und Lidocain-Krampfe. Arzneimittel-Forschung (Aulendorf). 23(4):545-549, 1973.

The anticonvulsant action of two benzodiazepines, chlorophenyl and clonazepam were investigated in male rabbits. Seizures were elicited by injection of lidocaine or topical application of penicillin on the cortex. Electroencephalographic criteria were used for the evaluation of the anticonvulsant activity. While both benzodiazepines exerted a qualitatively similar anticonvulsant action, they differed in their anticonvulsive potency: clonazepam was found to be more potent against both types of seizures. Higher doses of both benzodiazepines were needed to suppress the penicillin induced seizure activity and even with these doses not all phenomena of this seizure activity could be abolished completely. 40 references.

179985 Siemens, Albert J.; Kalant, Harold; Khanna, Jatinder M.; Marshman, Joan; Ho, Gregory. Department of Pharmacology, University of Toronto, Toronto, Canada **Effect of cannabis on pentobarbital-induced sleeping time and pentobarbital metabolism in the rat.** Biochemical Pharmacology (Oxford). 23(3):477-488, 1974.

The effects of two cannabis extracts with different cannabinoid compositions, as well as of pure delta1-tetrahydrocannabinol (THC), cannabinol (CBN) and cannabidiol (CBD), on pentobarbital metabolism were studied in the rat. Extract I, with high proportions of CBN and CBD relative to THC, when given by gavage 21.5, 40 or 63 hr before pentobarbital prolonged the sleeping time by 53%, 42% and 21% respectively. This effect was paralleled by decreases in the rate of disappearance of 014C0pentobarbital from the blood, and of pentobarbital metabolism by live microsomal preparations in vitro. Extract II, with low relative proportions of CBN and CBD, did not have any significant effect on pentobarbital metabolism or sleeping time. CBD alone, in the same dose as that given in Extract I, had very similar effects, while a dose of CBD equivalent to

that given in Extract II had no effect. THC, CBN and CBD added to normal rat liver microsomes in vitro inhibited pentobarbital metabolism competitively, CBD being a much more potent inhibitor than THC and CBN. The CBD content may, therefore, be a significant factor in interactions between marihuana and other drugs. 33 references. (Author abstract)

179986 Karoum, Farouk; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Excretion of norepinephrine and dopamine alcoholic metabolites after 6-hydroxydopamine.** Biochemical Pharmacology (Oxford). 23(3):533-538, 1974.

Urinary excretion of 4-hydroxy-3-methoxyphenylglycol(HMPG) and 4-hydroxy-3-methoxyphenylethanol (HMPE) sulfates (HMPG-SO4 and HMPE-SO4) and of their two glucuronides (HMPG-Gluc) and (HMPE-Gluc) were critically studied in normal and demedullated rats after 6-hydroxy-dopamine (6-HD) treatment. 6-HD hydrobromide (25 mg/kg) was administered either intravenously (chemical sympathectomy) or intraventricularly (central sympathectomy). Demedullation did not significantly change the output of any of the above conjugated metabolites. Chemical sympathectomy significantly reduced the excretion of HMPG-SO4 by about 40%. The other metabolites measured were not changed by chemical sympathectomy. Evidence was provided that indicated the presence in the peripheral sympathetic nervous system of nerve terminals resistant to destruction by 6-HD. These resistant nerve terminals were further shown to be involved in the production of HMPG-Gluc. Central sympathectomy fails to change the urinary excretion of the metabolites studied, including HMPG sulfate or glucuronide. 30 references. (Author abstract)

179992 Sabelli, Hector C.; Pedemonte, Walter A.; Whalley, Christopher; Mosnaim, A. David; Vazquez, Alfredo J. Department of Pharmacology, University of Health Sciences The Chicago Medical School, 2020 W. Ogden Avenue, Chicago, IL 60612 **Further evidence for a role of 2-phenylethylamine in the mode of action of delta9-tetrahydrocannabinol.** Life Sciences (Oxford). 14(1):149-156, 1974.

The role of 2-phenylethylamine (PEA) in the mode of action of delta9-tetrahydrocannabinol (THC) was examined in rabbits. THC increased the recovery of labeled PEA from brain following its intraventricular administration. THC also enhanced the excitatory effect of iontophoretic PEA on cortical unit potentials. Although THC induced sedation in mice, the subsequent injection of reserpine induced transient excitement. Low doses of PEA, which do not significantly alter the behavior of mice, induced marked excitement in mice pretreated with THC. In mice treated with pargyline, THC induced excitement (instead of sedation); this excitement was increased by PEA and reduced by phenylethanolamine. These results suggest that THC inhibits the disposition of PEA. Since endogenous PEA may be one of the adrenergic ergotropic modulators, it may play a role in the euphoriant effect of marihuana. 14 references.

180020 Hsu, Louise L.; Mandell, Arnold J. Dept. of Psychiatry, School of Medicine, Univ. of California, San Diego, La Jolla, CA 92037 **Stimulation of brain aromatic alkylamine N-methyltransferase activity by FAD and methylcobalamin.** Life Sciences (Oxford). 14(5):877-885, 1974.

The effects of methylcobalamin alone and with various reducing systems (FADH2, FAD or its analogues in combination with NADH or betamercaptoethanol) on the activity of partially purified aromatic alkylamine N-methyltransferase (AANMT) from rat brain was studied. The specific activity of AANMT in the presence of methylcobalamin alone was enhanced (125% of control). In the presence of FAD alone (but not FADH2 etc) it was 175% of control; and in the presence of methylcobalamin plus FAD plus betamercaptolethanol it reached 30% of control. Preliminary evidence suggests that FAD induces allosteric kinetics for the activated enzyme with respect to the methyl donor 5-methyltetrahydrofolic acid. 15 references. (Author abstract modified)

180022 Jacoby, Jacob H.; Lytle, Loy D.; Nelson, Mark F. Dept. of Nutrition and Food Science, Massachusetts Institute of Technology, Cambridge, MA 02139 **Long-term effects of 5,7-dihydroxytryptamine on brain monoamines.** Life Sciences (Oxford). 14(5):909-919, 1974.

Long-term effects of 5,7-dihydroxytryptamine (5,7-DHT) on brain monoamines were examined in rats. 5,7-DHT was injected intraventricularly in adult male rats; animals were killed at various times after the injection and brains were examined for changes in the concentration of tryptophan, serotonin, 5-hydroxyindole acetic acid, norepinephrine and dopamine. Brain 5-hydroxyin-

dolamines were markedly depleted at all time periods examined, even after the administration of a tryptophan load. A small but significant decline in brain norepinephrine but not dopamine was also noted after the administration of the dihydroxytryptamine. 18 references. (Author abstract modified)

180057 Anderson, Pamela F.; Jackson, D. M.; Chesher, G. B. Department of Pharmacology, University of Sydney, Sydney, NSW 2006, Australia **Interaction of delta9-tetrahydrocannabinol and cannabidiol on intestinal motility in mice.** Journal of Pharmacy and Pharmacology (London). 26(2):136-137, 1974.

The effects of cannabinoids on intestinal motility in SW strain mice are reported and describe an interaction between cannabidiol and delta9-tetrahydrocannabinol (delta9-THC). A combination of 10mg each delta9-THC and cannabidiol per kg produces a greater depression of intestinal motility than does 20mg. The combination of 10mg delta9-THC with 40mg cannabidiol per kg produces a depressant effect equal to about 40mg delta9-THC per kg. The interaction is considered to be additive rather than synergistic. The results indicate that the effect of cannabis extract on intestinal motility is influenced by the ratio of cannabinoids it contains. The importance of defining the composition of cannabis extracts in terms of all the major cannabinoids rather than of delta9-THC alone is emphasized. 8 references.

180058 Andjelkovic, Draginja. Department of Pharmacology, PF 662, Medical Faculty, Belgrade 11 000, Yugoslavia **Effect of adrenergic substances on oxygen consumption of rat brain tissue.** Journal of Pharmacy and Pharmacology (London). 26(2):138-139, 1974.

The effects of noradrenaline, adrenaline and isoprenaline on the oxygen consumption of rat brain were studied. Results show that adrenaline and isoprenaline, substances acting on beta-adrenoceptors stimulate the cellular respiration of cortical slices, whereas noradrenaline does not. Propranolol completely abolishes stimulation of oxygen consumption caused by adrenaline and isoprenaline. These findings indicate that the stimulation of oxygen uptake of rat brain cortical tissue by isoprenaline and adrenaline is the response of stimulation of beta-adrenoceptors. 2 references.

180059 Braestrup, C. Central Laboratory, Sct Hans Hospital, Dept. E, DK-4000 Roskilde, Denmark **Effects of phenoxybenzamine, aceperone and clonidine on the level of 3-methoxy-4-hydroxyphenylglycol (MOPEG) in rat brain.** Journal of Pharmacy and Pharmacology (London). 26(2):139-141, 1974.

The effect of the alpha-adrenoceptor antagonists, aceperone and phenoxybenzamine, and alpha-adrenoceptor agonist, clonidine, on the level of 3-methoxy-4-hydroxyphenlyglycol (MOPEG) in the CNS of male Wistar rats was studied. The results indicate that the alpha-adrenoceptor antagonists phenoxybenzamine and aceperone increase noradrenaline release, while the alpha-adrenoceptor agonist clonidine decreases noradrenaline release in the CNS of rats. The results thus agree with the contention that the activity of noradrenergic neurons is compensatorily regulated following blockade or stimulation of the alpha-adrenoceptors in the CNS of rats. 21 references.

180060 Miller, R. J.; Iversen, L. L. MRC Neurochemical Pharmacology Unit, Department of Pharmacology, Medical School, Hills Road, Cambridge CB2 2QD, England **Effect of chlorpromazine and some of its metabolites on the dopamine-sensitive adenylate cyclase of rat brain striatum.** Journal of Pharmacy and Pharmacology (London). 26(2):142-144, 1974.

The effect of chlorpromazine and some of its major metabolites on the dopamine stimulated increase in cyclic AMP production male Wistar rat striatal homogenates was examined. The mono and bis-desmethyl derivatives of chlorpromazine and to a lesser extent 7-hydroxy-chlorpromazine blocks the effect of dopamine on cyclic AMP levels but are less potent than chlorpromazine. The results support the findings that these metabolites increase dopamine turnover in mouse brain. It appears that several metabolites may play a direct role in chlorpromazine clinical and neuroleptic action. 14 references.

180096 Martin, Yvonne C.; Holland, James B.; Jarboe, Charles H.; Plotnikoff, Nicholas. Experimental Therapy Div., Abbott Laboratories, North Chicago, IL 60064 **Discriminant analysis of the relationship between physical properties and the inhibition of monoamine oxidase by aminotetralins and aminoindans.** Journal of Medicinal Chemistry. 17(4):409-413, 1974.

A discriminant analysis of the relationship between the physical properties and the inhibition of monoamine oxidase (MAO) by aminotetralins and aminoindans was made. N-Methyl-5-methoxy-1-indanamine, N-ethyl-5-methoxy-1-tetralinamine and 5-methoxy-1-tetralinamine and 6-methoxy-1-tetralinamine are potent inhibitors of mouse MAO at 100mg/kg po. Discriminant analysis of 20 analogs of these compounds suggests that the size of the amine substituent as well as the position of methoxyl substitution influences in vivo potency. A full discussion and a tabular report of the structure, physical properties and the MAO inhibitory potency of the compounds is included. 13 references. (Author abstract modified).

180097 Felix, Arthur M.; Winter, Donald P.; Wang, Su-Sun; Kulesha, Irina Douvan; Pool, William R.; Hane, Dorothy L.; Sheppard, Herbert. Dept. of Chemical Research, Hoffman-La Roche Inc., Nutley, NJ 07110 **Synthesis and antireserpine activity of peptides of L-Dopa.** Journal of Medicinal Chemistry. 17(4):422-426, 1974.

A series of dipeptides and tripeptides containing L-Dopa was prepared and examined for antiParkinson activity in mice. Some of the peptides were more effective in reversing reserpine induced catatonia than L-Dopa. The peptides were relatively nontoxic and resulted in a low degree of stereotypic behavior. 17 references. (Author abstract).

180507 Shin, Kyung Chu L; Cheon, Yun Suk. Dept. of Pharmacology, College of Medicine, Korea Univ., Seoul, Korea **Influences of reserpine and chlorpromazine on the analgesic and metabolic effects of morphine.** Korea University Medical Journal (Seoul). 10(3):653-661, 1973.

The influences of reserpine (R) and chlorpromazine (CP) on the analgesic and metabolic effects of morphine were investigated using the hot plate reaction time test in mice and by measuring the changes in the blood sugar content and serum transaminase activities (S-GOT, S-GPT) in rabbits. Animals were pretreated with R 24 h before and with CP 30 min prior to study. Results showed that: the analgesic effects of morphine were inhibited by R but augmented by CP; the hyperglycemic effects of morphine were augmented by R but inhibited by CP; the S-GOt, S-GPT activities induced by morphine were inhibited by R but augmented by CP; and R and CP not only act contrary to the analgesic effect of morphine but act differently on the changes of blood sugar level and serum transaminase activities induced by morphine. 37 references. (Author abstract modified)

180582 Cheney, D. L.; Costa, E.; Hanin, I.; Racagni, G.; Trabucchi, M. St. Elizabeths Hospital, NIMH, Washington, DC **Acetylcholine turnover in brain of mice and rats: effects of various dose regimens of morphine. (Unpublished paper).** Bethesda, MD, NIMH, 1974. 12 p.

The dynamics of the cholinergic system was studied in mice and rats by measuring the brain acetycholine (ACh) turnover rate after a single injection of morphine, after development of physical dependence upon morphine, and during naloxone precipitated withdrawal. It is shown that ACh turnover is affected differently in different species. Analysis of the turnover rate in mouse brain, rat striatum and occipital cortex from animals receiving a large dose of morphine or implanted chronically with morphine pellets reveal different actions of morphine on ACh synthesis. A single injection of morphine did not affect turnover measured in the mouse brain or the rat striatum but reduced the synthesis of ACh in rat occipital cortex ACh. Chronic morphine treatment increased whole mouse brain ACh turnover, decreased rat caudata ACh turnover, and failed to alter the ACh turnover in rat cortex. Finally, naloxone reversed the changes of ACh turnover elicited by morphine although naloxone is devoid of any effect on the synthesis of ACh in mice and rat brains. 25 references. (Author abstract modified)

180723 Chanal, J.-L.; Marignan, R.; Cousse, H.; Baldet, M. Laboratoire de Physique, Faculte de Pharmacie, 34-Montpellier, France **/Study with radiotracers of the distribution of a new psychotrope in mice: L-2-pyrrolidone-5-carboxylate dimethylaminoethanol. I. Comparison with L-glutamic and L-2-pyrrolidone-5-carboxylic acid.** Etude par radiotraceurs de la distribution chez la Souris d'un nouveau psychotrope: le L-2-pyrrolidone-5-carboxylate de dimethylaminoethanol. I. Comparison avec les acides L-glutamique et L-2-pyrrolidone-5-carboxylique. Therapie (Pairs). 27(1):35-46, 1972.

The absorption and distribution of a new psychotrope, the L-2-pyrrolidone-5-carboxylate of dimethylaminoethanol was examined in mice using autoradiography. After oral administration of the compound, the uptake and elimination in mice was assessed via autoradiographs of sagittal

sections and by measuring radioactivity at different organs. Absorption of this drug significantly exceeded that of L-glutamic acid used as a reference. 8 references. (Author abstract modified)

181467 Berndt, S.; Schwabe, U. Institut fur Pharmakologie, Medizinische Hochschule, Hannover, Roderbruchstr. 101, 3000 Hannover-Kleefeld, Germany **Effects of neuroleptics and thymoleptics on phosphodiesterase activity and on cyclic 3',5'-AMP levels in rat brain.** Archives of Pharmacology (Berlin). 274(Supplement):R18, 1972.

A study of neuroleptics and thymoleptics on phosphodiesterase (PDE) activity in vitro and on cyclic adenosine 3',5'-monophosphate (cAMP) content of rat brain in vivo, which found that the inhibition of PDE by psychotropic drugs is obviously of minor importance for the observed accumulation of cAMP and is not directly related to the psychopharmacological effects of these agents, is presented. Chlorpromazine, triflupromazine, and chlorprothixene inhibited PDE in a noncompetitive manner, whereas imipramine, desipramine, and amitryptiline proved to be competitive inhibitors. Haloperidol had virtually no effect on PDE activity. (Journal abstract modified).

181468 Brandau, K.; Axelrod, J. Farbenfabriken Bayer AG, Institut fur Pharmakologie, Friedrich-Ebert-Str. 217, 56 Wuppertal 1, Germany **The biosynthesis of the co-neurotransmitter octopamine in comparison with the neurotransmitter noradrenaline.** Archives of Pharmacology (Berlin). 274(Supplement):R21, 1972.

The hypothesis was examined that octopamine, because of its normal occurence in sympathetic nerves, is a coneurotransmitter with the neurotransmitter noraderaline. Endogenous concentrations of octopamine in the hearts and brains of rats were measured and it was found that octopamine is synthetized by the same enzymes as noradrenaline. It was also found that the same biosynthetic precursors, except tyramine, were used. Previous results, which showed ring hydroxylation of octopamine forming noradrenaline, are related to data showing that dopamine and 3,4-dihydroxyphenylalanine (DOPA) can be ring dehydroxylated in the brain of rats. The pharmacological relevancy of these findings concerning the treatment of Parkinsonism and hepatic coma with L-dopa is interpreted. (Journal abstract modified).

181469 Kilian, Marion; Frey, H.-H. Inst. f. Vet.-Pharmakol. u. Toxikol., Freie Univ., Koserstr. 20, D-1000 Berlin 33, Germany **Significance of the central biogenic amines for the threshold in electro and pentetrazole seizures.** Archives of Pharmacology (Berlin). 274(Supplement):R65, 1972.

The effects of the central biogenic amines in elevating or lowering the threshold in electroconvulsions and pentetrazole seizures in mice and rats are studied. This suggests a role of 5-hydroxytryptamine (5-HT) and noradrenaline metabolism in both seizure models while dopamine appears to be of minor importance. In both species, electroconvulsive threshold was elevated by pretreatment with 5-hydroxytryptopan (5-HTP) or L-dopa and lowered after pretreatment with p-chlorophenylalanine, alpha-methyltyrosine, disulfiram, or FLA-63. The threshold was also lowered by cyproheptadine and phentolamine but not by haloperidol. Pentetrazole threshold for clonic convulsions was altered in the same direction as that for electroconvulsions by 5-HTP, alpha-methyltyrosine, disulfiram, and FLA-63, but p-chlorophenylalanine, cyproheptadine, and alpha-adrenolytics were without effect. The threshold for the tonic component of the chemoseizure was predominantly altered by manipulations on the tryptaminergic side. (Journal abstract modified).

181470 Krieglstein, G.; Hahn, I.; Krieglstein, J.; Tschentscher, K. Pharmakologisches Institut der Universitat Mainz, Obere Zahlbacher Str. 67, D-6500 Mainz, Germany **Influence of various drugs on the binding of chlorpromazine to erythrocytes and albumin.** Archives of Pharmacology (Berlin). 274(Supplement):R70, 1972.

The binding of the highly lipophilic chlorpromazine (CPZ) to erythrocytes and albumin under the influence of various drugs in a simplified blood was studied. Evidence is presented that salicylic acid and impramine do not displace CPZ from albumin binding, as reported in the literature, in the simplified blood used. It is concluded that binding studies merely with albumin solutions or plasma may be misleading when pharmacokinetic implications are argued. (Journal abstract modified).

181471 Maitre, L.; Baumann, P.; Staehelin, M. Biologische Forschungslaboratorien, Division Pharmazeutika, CIBA-GEIGY AG, CH 4002 Basel, Switzerland **Catecholamine turnover in the rat brain: different results obtained in different experimental conditions.** Archives of Pharmacology (Berlin). 274(Supplement):R76, 1972.

The effects of chlorpromazine (CPZ) and benzoctamine were compared in three systems used for studying catecholamine (CA) turnover in the rat brain. The systems were: accumulation and release of 3H-CA formed from intravenously injected 3H-tyrosine; accumulation of 3H-CA in brain slices incubated with 3H-tyrosine; and depletion rate of the endogenous CA stores after blockade of CA biosynthesis with alpha-methyltyrosine. The results show a good correlation between methods involving newly synthesized CA and a profound discrepancy between those models that use blockade of CA biosynthesis. It is suggested that different CA pools are measured in the two sets of experimental conditions. (Journal abstract modified).

181575 Dalton, Colin; Crowley, Herman J.; Sheppard, Herbert; Schallek, William. Dept. of Cell Biology, Hoffman-La Roche, Inc., Nutley, NJ 07110 **Regional cyclic nucleotides phosphodiesterase activity in cat central nervous system: effects of benzodiazepines.** Proceedings of the Society for Experimental Biology and Medicine. 145(2):407-410, 1974.

A possible correlation between phosphodiesterase (PD) inhibition and regional pharmacological activity was investigated in the central nervous system (CNS) of the cat. Cyclic adenosine 3',5'-monophosphate (cAMP) and cyclic guanosine 3'5'-monophosphate (cGMP) activity was found in the supernatant fraction of 15 freshly dissected regions of the cat CNS. Activity was highest in the cerebral cortex. Lesser activity was observed in other regions of the CNS. Diazepam and medazepam hydrochloric acid were as active as the known cAMP PD inhibitors papaverine and dipyridamole in cat cortex, rat brain and mouse neuroblastoma cells. The diazepam metabolites N-demethyldizepam, N-methyloxazepam, and oxazepam showed less inhibition of PD than the parent compound. No evidence was found for a regionally specific biochemical action of the benzodiazepines involving intracellular cAMP or cGMP. 10 references. (Author abstract modified)

181576 Lorenz, Robert J.; Branch, Berrilyn J.; Taylor, Anna Newman. Dept. of Anatomy, UCLA School of Medicine, Los Angeles, CA 90024 **Ontogenesis of circadian pituitary-adrenal periodicity in rats affected by neonatal treatment with ACTH.** Proceedings of the Society for Experimental Biology and Medicine. 145(2):528-532, 1974.

The effect of neonatal treatment with adrenocorticotropic hormone (ACTH) on circadian corticosteroid rhythm was studied in rats. Treatment on days 7 to 9 and 17 to 19 suppressed circadian corticosteroid rhythm in adult rats. Treatment with gel vehicle at these ages, except in females on days 17 to 19, or neonatally, did not produce similar effects. Thus, brief exposure to high circulating levels of ACTH at two critical neonatal periods affects the normal development of mechanisms underlying cyclic pituitary adrenal function in the rat. 13 references. (Author abstract modified)

181593 Sawada, Hideo; Yano, Hiroko; Hara, Akira; Kido, Akira; Fukumoto, Masaru. Department of Legal Medicine, Gifu University School of Medicine, Japan **Studies on metabolism of bromazepam (II): colorimetric determination and metabolic fate of bromazepam in animals.** ACTA Scholae Medicinalis Universitatis in Gifu (Gifu). 20(6):608-618, 1972.

A method for the colorimetric determination of bromazepam (BZ) in pharmaceutical preparations, urine and serum is described. By hydrolysis with hydrochloric acid, BZ becomes 1-amino-5-bromobenzoylpyridine (ABBP), which is color developed by the Bratton-Marchall method. The excretion of BZ and ABBP in animal urine orally administered a single dose of BZ was observed at 25% of the administered dosage in the 2mg/kg group of rabbits. To observe the distribution of BZ in rabbits, BZ was administered to 20mg/kg and 100mg/kg groups. The concentration of BZ in each tissue in the 10mg/kg group was observed to be high in bile, testicles, liver, kidney, spleen, lung, and brain in order of increasing concentration, and in the 100mg/kg group, bile, liver, kidney, brain, spleen and lung. In both groups, the highest concentration was observed in the liver. In the contents in gastrointestines, it was the highest in the stomach. 15 references. (Author abstract modified)

181650 Kimishima, Kenjiro; Yamazaki, Michiyo; Tanabe, Kyoko; Ogura, Chikara. Department of Pharmacology, Tottori University School of Medicine, Yonago, Japan **Central nervous action of bromazepam, a new benzodiazepine derivative.** Journal of the Yonago Medical Association (Yonago). 23(2):107-116, 1972.

The effects of bromazepam on the central nervous system were analyzed in mice, rats, rabbits and cats. Diazepam and nitrazepam were used as

control materials. Following intraperitoneal administrations of bromazepam in chronically implanted rabbits, electroencephalographic properties in spontaneous electroencephalograms, such as slow waves with high amplitudes in the neocortex, were distinguished. The arousal responses by stimulation of the hypothalamus and midbrain reticular formation and the seizure discharges produced by stimulation of the amygdala were inhibited. In the experiments in which motor activities and pentetrazol induced convulsions were used as indices, any liability to produce the dependence was not noticed even by continuous administrations of bromazepam up to 25 days. 16 references. (Author abstract modified)

181809 Dorris, R. L.; Shore, Parkhurst A. Department of Pharmacology, University of Texas Southwestern Medical School, Dallas, TX 75235 **Interaction of apomorphine, neuroleptics and stimulants with alpha-methyl-m-tyramine, a false dopaminergic transmitter.** Biochemical Pharmacology (Oxford). 23(4):867-872, 1974.

The interactions of apomorphine, neuroleptics and stimulants with alpha-methyl-m-tyrosine (MMTA), a false dopaminergic transmitter were studied. The rate of decline of MMTA from the corpus striatum of the rat can be altered by drugs acting on the dopamine (DA) receptor. By the use of this false dopaminergic transmitter, amine release by drugs acting directly on the neuron can be distinguished from that by drugs acting indirectly via DA receptor interaction. The rate of disappearance of MMTA is much slower than that of DA after tyrosine hydroxylase inhibition, but the combination of synthesis blockade and monoamine oxidase blockade greatly slowed the rate of DA decline, suggesting that normally much DA is metabolized intraneuronally. The decline rate of MMTA appears to accurately reflect the striatal DA neuron impulse flow rate under normal conditions or after administration of drugs which act only to alter impulse flow. 12 references. (Author abstract)

181810 Colburn, Robert W.; Ng, Lorenz K. Y.; Lemberger, Louis; Kopin, Irwin J. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Subcellular distribution of delta9-tetrahydrocannabinol in rat brain.** Biochemical Pharmacology (Oxford). 23(4):873-877, 1974.

delta9-Tetrahydrocannabinol-3H (THC), administered intracisternally, was distributed almost equally among particulate fractions of rat brain homogenates with only a small proportion in the supernatant fraction. Similar distribution of THC-3H was found when the drug was added directly to brain homogenates. Most of the metabolites of THC-3H, however, were found in the supernatant fraction, but synaptosomes retained significantly greater amounts of polar metabolites than do other particulate fractions. After incubation with synaptosomes in vitro, exceptionally high tissue/medium ratios were found for delta9-THC-3H accumulation. This accumulation was not prevented by metabolic inhibitors and was not temperature dependent. The results indicate that significant amounts of THC and its polar metabolites can be concentrated in synaptosomes by nature of the drug's lipophilic properties. 17 references. (Author abstract)

181813 Dembert, Mark L.; Harclerode, Jack. Jefferson Medical College, Philadelphia, PA **Effects of l-delta9-tetrahydrocannabinol, dl-amphetamine and pentobarbital on oxygen consumption by mouse brain and heart homogenates.** Biochemical Pharmacology (Oxford). 23(5):947-956, 1974.

Using a polarographic method (oxygen electrode), the effects of l-delta9-tetrahydrocannabinol, DL-amphetamine and pentobarbital were compared in regard to their action on oxygen consumption by mouse brain and heart homogenates. This study was unique in that the drugs were injected in vivo, while measurement of oxygen consumption was conducted in vitro for up to 8 hr. This allowed for the true active forms of these drugs -- after normal biotransformation, if necessary -- to exert the effects later measured. Pentobarbital was found to have no significant effect on cerebral or cardiac oxygen comsumption. Both DL-amphetamine and l-delta9-tetrahydrocannabinol caused significant stimulation of oxygen consumption in the brain and heart for up to at least 2.5hr after administration. This could indicate that both drugs cause increased synthesis and utilization of high energy compounds (i.e. ATP) via oxidative phosphorylation in the two organs. However, DL-amphetamine and l-delta9-tetrahydrocannabinol also induced limited depression of oxygen consumption in the brain and heart, respectively, at 8 hr after administration. 39 references. (Author abstract)

181815 Radulovacki, M.; Brunngraber, E. G. Department of Pharmacology, University of Illinois, College of Medicine, Chicago, IL 60680 **Convulsion-producing property of the dialyzable glycopep-**

tide preparation from whole rat brain. Neuropharmacology (Oxford). 13(2):139-142, 1974.

A dialyzable preparation containing whole rat brain glycopeptides caused clonic - tonic convulsions when administered intraventricularly to cats. It was suggested that this effect is due to a glycopeptide recovered from a brain glycoprotein or glycoproteins. 6 references. (Author abstract)

181818 Joy, R. M. Department of Physiological Sciences, School of Veterinary Medicine, University of California, Davis, CA 95616 **Alteration of sensory and motor evoked responses by dieldrin.** Neuropharmacology (Oxford). 13(2):93-110, 1974.

The alteration of sensory and motor response evoked by dieldrin was examined. Dieldrin has specific effects on responses evoked to peripheral by central stimuli. Postsynaptic components of cortical responses to any modality of sensory stimulation are facilitated by dieldrin while subcortical potentials are moderately depressed. Similar postsynaptic facilitation occurs with direct cortical and transcallosal stimulation. In contrast to these findings, cortical and peduncular responses to stimulating fibres in the brachium conjunctivum or at ventralis lateralis were moderately depressed. With dieldrin a late positive - negative potential developed over frontal cortical areas which was indistinguishable from the irradiation potential produced by metrazol. The late wave was the source of the spike discharges that developed in the electroencephalographic (EEG) records. The close similarities observed between dieldrin and metrazol strengthen the hypothesis that they share either a common mechanism or final common pathways responsible for electrophysiological events. Differences in reports of these agents seem more readily explained in terms of their different pharmacokinetic properties. 51 references. (Author abstract)

181941 Jones, Gareth; Pertwee, Roger G.; Gill, Edward W.; Paton, William D. M. Faculty of Pharmacy, Box 6804, 113 86 Stockholm, Sweden **Relative pharmacological potency in mice of optical isomers of delta1-tetrahydrocannabinol.** Biochemical Pharmacology (Oxford). 23(2):439-446, 1974.

The relative pharmacological potency in mice of optical isomers of tetrahydrocannabinol (THC) was studied. The (+)-delta1-THC was found to be significantly less potent than the levortatory isomer, the mean potency ratio being 13. Brain levels of (+)-delta1-THC and its metabolites were measured in mice 20 min after intravenous injection of 3H-(+)-delta1-THC and were compared with the corresponding levels of (-)-delta1-THC and its metabolites. With the exception of the concentrations of one metabolite, no differences were observed between the mean levels of enantiomorphs of the cannabinoids in the brain. In the case of the single metabolite the brain level of the dextrorotatory isomer was higher than that of the levorotatory isomer. It was concluded that the differences in the psychopharmacological potencies in vivo of the optical isomers of delta1-THC are determined within the central nervous system and are not due to gross differences in metabolism or body distribution. 25 references. (Author abstract modified)

181942 Dewar, Arthur J.; Reading, Harold W. M.R.C. Brain Metabolism Unit, Department of Pharmacology, University of Edinburgh, 1 George Square, Edinburgh EH8 9JZ, Scotland **Effects of lithium on cerebral RNA metabolism in vitro and in vivo.** Biochemical Pharmacology (Oxford). 23(2):369-380, 1974.

The effect of lithium (Li) on cerebral ribonucleic acid (RNA) metabolism was studied in rats. Li could not replace Mg2 as an essential cofactor for RNA polymerase but stimulated the enzyme in the presence of optimum concentrations of Mg2. The stimulation was less than that achieved with Na and K and differed from these in being biphasic with respect to concentration. A similar biphasic effect of Li was seen with liver RNA polymerase and brain Poly C synthetase. The action of Li on pancreatic and brain ribonuclease resembled that of Na. Li did not reduce the inhibitory effect of Mg2. Chronic LiCl treatment in rats did not significantly alter the rate of RNA synthesis, the RNA content nor RNA composition in the brain. It is concluded that the changes in uric acid excretion in human manic depressives during lithium induced remission are not reflections of a direct or indirect effect of Li on cerebral RNA metabolism. 47 references. (Author abstract)

181944 Seiler, Nikolaus; Demisch, Lothar. Max-Planck Institut fur Hirnforschung, Arbeitsgruppe Neurochemie, Frankfurt/M-Niederrad, Germany **Oxidative metabolism of mescaline in the central nervous system -- IV: in vivo metabolism of mescaline and 2,3,4-trimethoxy-beta-phenylethylamine.** Biochemical Pharmacology (Oxford). 23(2):273-287, 1974.

Metabolic rates of mescaline (3,4,5-trimethoxy-beta-phenylethylamine) and of its nonhallucinogenic isomer, 2,3,4-trimethoxy-beta-phenylethylamine were studied in whole and in different areas of mouse brain in vivo. The effects of pargyline and of probenecid on the concentrations of the amines and their corresponding metabolites, together with the results obtained from intraventricular injections of mescaline suggested the formation of the trimethoxyphenylacetic acids in the brain. The metabolic differences between mescaline and 2,3,4-trimethoxy-beta-phenylethylamine are discussed in terms of possible implications of metabolic parameters with psychotomimetic activity. 48 references. (Author abstract)

181945 Peters, David A. V. Department of Pharmacology, Faculty of Medicine, University of Ottawa, Ottawa, Canada **Comparison of the chronic and acute effects of D-lysergic acid diethylamide (LSD) treatment on rat brain serotonin and norepinephrine.** Biochemical Pharmacology (Oxford). 23(2):231-237, 1974.

The effects of repeated administration of small doses of d-lysergic acid diethylamide (LSD) on brainstem norepinephrine (NE), serotonin (5-HT), 5-hydroxyindoleacetic acid (5-HIAA), tyrosine, tryptophan, tyrosine hydroxylase and tryptophan hydroxylase have been studied in male rats. A daily dose of 20 micrograms/kg given for 14 days resulted in a significantly lowered NE level and tyrosine hydroxylase activity measured 24 hr after the last injection. Treatment with 100 micrograms/kg/day for the same period of time produced similar changes together with a significantly lower brainstem tyrosine content. Evidence was obtained that the NE turnover in rat brainstem was significantly increased at the higher dose level only. The lower dose of 20 micrograms/kg/day also resulted in an elevated 5-HT and lowered 5-HIAA content. However, when the dose was increased to 100 micrograms/kg/day the 5-HT content was unchanged and the 5-HIAA content increased. The 5-HT turnover was reduced when the rats were treated with 20 micrograms/kg/day but significantly elevated when the 100 microgram dose was used. 44 references. (Author abstract)

182088 Rand, Michael J.; Allen, Gary S.; Story, David F.; Varma, Bijoy. Department of Pharmacology, University of Melbourne, Parkville, 3052, Victoria, Australia **Effects of cholinomimetics on adrenergic transmission.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):10, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the effects of cholinomimetics on adrenergic transmission were reported. Experiments have been carried out with isolated artery segments from the rabbit ear and guinea pig atria. The cholinomimetic drugs studied were ACh, methacholine (MeCH), DMPP and MCN-A-343. In the artery preparation, ACh in very low concentrations increased responses to sympathetic nerve stimulation at low frequencies. DMPP blocked contractions and NA release in response to sympathetic nerve stimulation at high and low frequencies, but these effects were not antagonized by atropine. The findings suggest that there are differences between tissues in the pharmacological reactivity of adrenergic terminal axons. The effects of cholinomimetics are complex; nicotinic agonists cause NA release; muscarinic agonists inhibit NA release in response to nerve stimulation; muscarinic agonists in the presence of atropine may facilitate NA release; some cholinomimetics inhibit NA uptake. (Author abstract modified)

182089 Oka, Motoo. 2nd Department of Pharmacology, Faculty of Medicine, Osaka University, Osaka, Japan **The effects of drugs on the release of catecholamine.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum): 9, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the effects of drugs on the release of catecholamine (CA) from both adrenergically innervated organs and adrenal medullary tissue were examined. 14C-dopamine, 14C-DOPA or 14C-tyrosine in guinea-pig heart slices or vas deferens was released by acetylcholine (ACh) or excess K+ in the presence of Ca++ in the medium. This stimulated release of 14C-NA was markedly inhibited by the presence of a reduced concentration of Ca++ and was significantly inhibited when bretylium, bethanidine or guanethidine was present in the medium. The inhibition by these drugs could be antagonized by increasing the Ca++ concentration in the medium. Furthermore, it was found that when preparations of heart slices or vas deferens were incubated with 14C-tyrosine or 14C-DOPA, bretylium and bethanidine, but not guanethidine, significantly increased the accumulation of 14C-dopamine and decreased the formation of 14C-

deaminated metabolites, due to their inhibitory effects on MAO activity. Reserpine, which released NA, was found to increase MAO activity, presumably because it affected the mitochondrial membrane or structure in such a way as to increase penetration of NA into mitochondrial MAO. (Author abstract modified)

182091 Iida, Shoichi; Shimizu, Shin-ichiro. Department of Pharmacology, School of Dentistry, Hokkaido University, Sapporo, Japan **L-dopa and potentiation of alcohol anesthesia by chlorpromazine.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):69, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the potentiation of alcohol by chlorpromazine (CPZ) was examined in relation to true (nonmetabolic) potentiation. Alcohol was injected into rabbits at a dose of 1.5g/kg and a practically inactive dose of CPZ was also injected via the ear vein. A prolonged duration of the loss of corneal reflex resulting from alcohol by pretreatment with CPZ was considered as the potentiation. The anesthetic effect induced by rapid administration of alcohol was potentiated by CPZ at 1mg/kg or higher. Potentiation of alcohol by CPZ, in spite of its rapid onset of action, was a phenomenon that required time to develop. When alcohol and CPZ were injected simultaneously, there was no indication of a response which would suggest potentiation. A marked potentiation was observed when the time interval between two injections was 20 minutes or more. The results suggest that catecholamines in the CNS may be considered to be involved in the potentiation of alcohol by CPZ. (Author abstract modified).

182092 Katsuda, Nobuo; Hori, Nobuaki. Department of Pharmacology, Faculty of Dentistry, Kyushu University, Fukuoka, Japan **Effect of procaine, lidocaine and pentobarbital on electrical activity of guinea-pig olfactory cortex in vitro.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum): 70, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the effects of procaine, lidocaine and pentobarbital on evoked electrical activity in slices from guinea pig olfactory cortex maintained in vitro were reported. The evoked response of prepiriform cortex to stimulation of the lateral olfactory tract was composed of a brief biphasic action potential of olfactory tract (TR) followed by a negative wave of about 20 msec duration (N wave) upon which one or two brief positive notches (PS) were superimposed. Effect of a drug was observed by changing the medium containing appropriate concentration of a drug in place of normal incubation medium. Low concentration of both procaine and lidocaine, which affected inconsistently on TR and reduced slightly the amplitude of N-wave, left PS almost unchanged. Pentobarbital, on the other hand, suppressed both N-wave and PS indiscriminately. Both the local anesthetics produced a distinct modification in the time course of posttetanic potentiation (PTP), which closely resembled that obtained in low calcium medium and was reversibly antagonized by the addition of CaCl2 into the bathing medium. The change of PTP in the presence of pentobarbital, however, differed from that by local anesthetics. It was suggested that the preferential site of action of local anesthetics might be on presynaptic structures and that of pentobarbital on postsynaptic ones. (Author abstract modified).

182093 Fujimori, Kannosuke; Iwamoto, Takio. Department of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo, Japan **Studies on central regulating mechanism of the hypoglycemia induced by intraventricular administration of chlorpromazine.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):71, 1972.

At the 45th meeting of the Japanese Pharmacological Society, it was reported that intraventricular injection of chlorpromazine(CPZ) caused hyperglycemia in the rat and this hyperglycemia was depressed by simultaneous administration of dopamine. The mechanism of the CPZ induced hyperglycemia and its regulation in CNS were studied. Using antiinsulin serum it was shown that the depressive effect of dopamine on CPZ induced hyperglycemia was not caused by insulin. Hexamethonium blocked the CPZ induced hyperglycemia. 6-Hydroxydopamine (intraventricular) depleted brain catecholamines and caused a dose dependent reduction of CPZ induced hyperglycemia. The reduced hyperglycemia caused by 6-hydroxydopamine was recovered by subsequent administration of dopamine. These results indicate that the CPZ induced hyperglycemia is caused by epinephrine released from adrenal medulla via cholinergic nerve. In the CNS the presence of two different nerves which have respective threshold to dopamine level was noted, the one is a stimulator of CPZ induced hyperglycemia and the other a

depressor of the former nerve. (Author abstract modified).

182094 Takagi, Hiroshi; Kimura, Kiyoshi; Kimura, Yutaka; Ohata, Katsuya. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto, Japan **The effects of intraventricularly administered catecholamines and serotonin on the reserpine-induced spike waves recorded from the medical nucleus trapezoides in the rabbit.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):75, 1972.

At the 45th meeting of the Japanese Pharmacological Society, it was reported that during paradoxical sleep (PS), distinct spike waves appeared in the medial nucleus Trapezoides(Trap. m.). When bursts of 10-20 waves appeared, rapid eye movement, twitches of vibrisae and extremities were seen. Spike waves similar to those observed during PS were recorded from Trap.m. after reserpine or p-chlorophenylalanine administration. In the preliminary experiment, it was shown that reserpine induced spike waves were markedly suppressed after ip injection of 5-hydrorytryptophan, but they were slightly suppressed after L-DOPA. Intravenous injection of alpha methylmetayrosine (MMT) suppressed these spike waves almost completely for 6 hrs and more. The effects of intraventricular administrations of various monoamines were investigated. 5-Hydroxytryptamine showed marked suppressive effect on the reserpine induced spike waves for 30-40 min after administration. The similar tendency was seen after noradrenaline, but only slight suppressive effect was seen after dopamine. Metaramino, a metabolite of MMT, showed showed long lasting and marked suppressive effect. (Author abstract modified).

182095 Watanabe, Shigenori; Nishi, Hiroyoshi; Ueki, Showa. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Sapporo, Japan **Electroencephalographic effects of delta9-tetrahydrocannabinol, LSD-25, mescaline and 2,5-dimethoxy-4-methylamphetamine in the rabbits.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):76, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the electroencephalographic (EEG) effects of delta9-tetrahydrocannabinol (THC), LSD-25, mescaline, and 2,5-dimethoxy-4-methylamphetamine (DOM) in unanesthetized unrestrained rabbits with chronic electrode implants were reported. THC caused a marked increase in high voltage slow waves in the spontaneous EEG of the neocortex, although the animals were rather hyperirritable without showing drowsiness in behavior. The change in the hippocampal EEG was the most characteristic change. DOM changed the EEG in all brain areas to an arousal pattern, simultaneously with behavioral arousal. Mescaline invariably caused a typical arousal pattern in the spontaneous EEG. LSD-25 decreased the voltage of the EEG in all brain areas. The recruiting response elicited by electrical stimulation of the centromedian thalamic nucleus was increased in voltage by THC, but slightly inhibited by the other drugs. The hippocampal afterdischarges were slightly increased in duration by DOM, mescaline and LSD-25, but were not altered by THC. (Author abstract modified).

182096 Yamamoto, Ken-ichi; Sawada, Tohru; Naito, Yukio; Utsumi, Shizuo. Shionogi Research Laboratory, Osaka, Japan **EEG characteristics in various species of animal and their relation to the CNS-effects of drugs.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):76, 1972.

At the 45th meeting of the Japanese Pharmacological Society, electroencephalographic (EEG) and behavioral studies carried out in several species of animal with chronically indwelling brain electrodes for the neuropharmacological analysis of sleep mechanisms and for the estimation of the sites of action of CNS affecting agents were reported. From the correspondence between (EEG) and behavior, normal EEG levels were classified into three levels in rats, five levels in rabbits, six levels in cats and dogs, and seven levels in monkeys. No species specificity was observed among the animals with reserpine and barbiturates. Benzodiazepines, chlorpromazine and morphine caused continuous sedateness and sleeping in dogs and monkeys, less slow waves in cats. Stable slow waves were elicited by benzodiazepines and morphine in flaxedil immobilized acute cats; but characteristic arousal patterns were caused by the same doses of the agents in chronic cats. Some kinds of phenothiazine derivatives and anticholinergic agents elicited stable slow waves and spindle bursts with eye opening behavior; at a surgically narcotic level, ether caused a desynchronized pattern. (Author abstract modified).

182097 Murayama, Satoshi; Uemura, Hiroko; Suzuki, Toshio. Department of Pharmacology,

School of Medicine, Chiba University, Chiba, Japan **Effects of benzodiazepines on spinal reflexes in cats.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):79, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the effects of benzodiazepines on spinal reflexes in unanesthetized spinal cats were reported. Monosynaptic and polysynaptic reflex potentials were recorded from ventral root, and the dorsal root reflex potential was recorded. The dorsal root potential was markedly decreased by small doses of picrotoxin but not by strychnine. Benzodiazepines increased the amplitude of dorsal root reflex potential; bromazepam showed especially remarkable effect. The order of the potency was, in decreasing order: bromazepam, diazepam, nitrazepam, flurazepam, oxazepam, medazepam and chlordiazepoxide. The administration of picrotoxin after benzodiazepines reversed the effects of benzodiazepines. Monosynaptic and polysynaptic reflex potentials were not so affected by the doses, which increased the dorsal root reflex potential, except oxazepam, which decreased monosynaptic and polysynaptic reflex potentials. Meprobamate and mephenesin reduced the amplitude of polysynaptic reflex and dorsal root reflex potentials. Chlorpromazine, amitriptyline and haloperidol showed not so remarkable effects on the response in the spinal preparation. These results suggest that benzodiazepines increase presynaptic inhibition. (Author abstract modified).

182099 Takenoshita, Mitsugu; Shimizu, Hirotoshi. First Department of Pharmacology, Kumamoto University Medical School, Kumamoto, Japan **A central effect of local anesthetics: prevention against the accumulation of cyclic AMP in brain slices.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):81, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the effects of local anesthetics, all of which are known to stabilize the membrane of peripheral sensory nerves, on the depolarizer elicited accumulation of cyclic AMP in brain slices were reported. Every anesthetic drug investigated was effective, at optimal concentrations, in producing more than 95% inhibition of the accumulation of cyclic AMP elicited with various depolarizing agents, e.g.,veratridine, ouabain, and high potassium ions. A series of dose activity study indicated that the order of the inhibitory potency was: dibucaine, tetracaine, cocaine, lidocaine, procaine. This is not consistent with the order of their local anesthetic potency. When compared on a basis of therapeutic doses, therefore, cocaine showed the strongest central effect in terms of the cyclic AMP level, followed by tetracaine, dibucaine, lidocaine, and procaine, in decreasing order. This order of biochemical action appears to be consonant with the order of their relative toxicity as the central stimulants, and would suggest that the central excitatory effect of local anesthetics might be due to their membrane stabilizing action on neuronal cells of (a particular area of) brain. (Author abstract modified).

182105 Sano, Mitsuaki; Shinohara, Masahiro; Wakamatsu, Yoshiko; Kobayashi, Masafumi; Sato, Mikio. Department of Pharmacology, Nihon University School of Dentistry, Tokyo, Japan **The influence of aldosterone or methamphetamine on liver glycogen deposition of mice stressed by long term isolation.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):93, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the effect of aldosterone (A) and methamphetamine (M) on liver glycogen deposition (LGD) and aggressiveness observed in male mice stressed with long-term isolation was reported. In the aggressiveness of A-mice, the first peak was observed at the fourth week (in higher degree than saline) and the second peak at the seventh week (in the same degree as S) and the second peak at the eigth week (in lower degree than saline). Glycogen deposition in liver of aggressive mice administered with A was more advanced than nonaggressive and aggregated mice treated with the same procedure. Glycogen deposition in the lower of isolated mice either aggressive or nonaggressive treated with M was more advanced than that of aggregated mice treated with the same, although the difference between the aggressive and nonaggressive mice was not significant. The glycogen deposition of aggregated mice treated with M was lower in comparison with saline. (Author abstract modified)

182113 Iwata, Heitaroh; Yamamoto, Itaru; Morita, Kyoji. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Osaka University, Osaka, Japan **Potentiation of barbiturate hypnosis by 5-diazoimidazole-4-carboxamide and its derivatives.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):97, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the potentiation of barbiturate hypnosis by 5-diazoimidazole-4-carboxamide (I) and 5-(3,3-dipropyl-1-triazeno)imidazole-4-carboxamide (II) were reported. Both compounds remarkably prolonged sleeping time induced with hexobarbital in mice, and thioazoimidazoles had more potent prolongating effect than their parent compound. II inhibited the liver hexobarbital metabolizing enzyme activity and delayed disappearance of the hypnotic from brain, while 5-(2-aminoethylthioazo)-4-carboxamide (III) had no effect on the metabolism and disappearance. The results suggest that prolongation of sleeping time by II may be due to the inhibition of hexobarbital metabolism. III probably potentiated barbiturate hypnosis by making the animals more sensitive to the hypnotic. Biological analysis has revealed that I had pharmacological properties like those of serotonin. The increase of serotonin content in mouse brain was also observed after the administration of III. (Author abstract modified)

182119 McGowan-Sass, B. K.; Timiras, P. S. Department of Physiology-Anatomy, UCB, Berkeley, CA 94720 **Modulatory effects of corticosteroids on evoked activity in the hippocampus and thalamus of the rat.** Federation Proceedings. 32(3):211, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the modulatory effects of corticosteroids on evoked activity in hippocampus and thalamus of the rat were reported. It has been hypothesized that glucocorticoids have a regulatory influence on incoming sensory signals. Several observations suggest that this modulation is mediated by the hippocampus: 1) the hippocampus is a primary site for corticoid uptake and release; 2) hippocampal stimulation influences changes in blood corticosteroid levels; 3) hippocampal lesions disrupt diurnal corticoid rhythms and affect taste thresholds; and 4) stimulation of the fimbria increases the amplitude of sensory evoked potentials. To test the hypothesis that the hippocampus modulates these changes in evoked activity, tactile and visual evoked potentials recorded from the hippocampus to those recorded from primary sensory areas in the thalamus in normal and adrenalectomized rats injected iv with corticosteroids were compared. In all subjects, corticoids caused a small but significant increase in amplitude of potentials in the thalamus, and a proportionately larger increase in potentials recorded from the hippocampus. Within the hippocampus, increases in amplitude due to corticoid administration were more long lasting in the ventral portion, while latencies were shorter in the dorsal portion. (Author abstract).

182121 Faingold, C. L.; Marrazzi, A. S. Department of Medical Science, Southern Illinois University Medical School, Springfield, IL 62708 **5-Hydroxytryptamine and histamine effects on reticulo-cerebellar evoked potentials.** Federation Proceedings. 32(3):221, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, 5-hydroxytryptamine (5-HT) and histamine (H) effects on reticulo-cerebellar evoked potentials were reported. Acute experiments were performed in the unanesthetized paralyzed cat. Studies showed that close arterial (vertebral) administration of 5-HT, or gamma aminobutyric acid produced a prompt and reversible depression of evoked potential amplitude. When the animals were pretreated with chlorpromazine the 5-HT induced depression was reversibly blocked, but the action of histamine was uneffected. The depressive effect of H was blocked by pretreatment with tripelennamine, but the action of 5-HT was uneffected. The findings on the reticulo-cerebellar pathway mirror the findings on the olivo-cerebellar as well as cortical and thalamic pathways and further extend the pharmacological generalization suggested by Marrazzi, et al. (Author abstract modified)

182123 Krebs, Helmut; Bindra, Dalbier. McGill University, Montreal 101, Quebec, Canada **Effects of neuropharmacological agents on hypothalamic neuronal activity: a microelectrophoretic study.** Federation Proceedings. 32(3):221, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the responsiveness of 277 identified neurons in the perifornical area and the ventromedial nucleus investigated in curarized rats through microelectrophoretic application of norepinephrine (NE), acetylcholine (ACh), amphetamine (Amph), and glucose (Glu) at the sites of extracellular unit recording were reported. The chemicals had varied effects, which depended on the specific site at which neurons were located. The parallels and the lack of parallels in the effects of NE, Amph, and Glu on the same neurons suggested that chemical coding of the feeding function involves, apart from any transmitter substance, the additional factor of a chemoceptive profile of

neurons. The results are consistent with the idea that NE may be a transmitter agent for certain hypothalamic neurons, but do not support the existing hypotheses attributing specific roles to NE and ACh in eating and drinking (Author abstract modified)

182124 Ward, John W.; Hash, Avery M., Jr.; Johnson, David N.; Funderburk, William H. A. H. Robins Research Laboratories, Richmond, VA 23220 **Pharmacologic analysis of the caudate spindle in cats.** Federation Proceedings. 32(3):247, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, an attempt to elucidate the transmitter involved in the caudate spindle response to a single, high intensity pulse was reported. A variety of drugs were used in acute and chronically prepared cats. Muscarinic blocking agents, atropine and scopolamine, and a nicotinic blocking agent, mecamylamine, had little direct effect on the spindling. Benactyzine, benztropine, and trihexyphenidyl also had no effect on the evoked response. Adrenergic involvement was ruled out by the use of alpha-adrenergic blocking agents, AHR-1900 and phentolamine, and by the beta-blockers propanolol and sotalol. p-Chlorophenylalanine had no effect on the spindles three days after administration, apparently precluding a role for serotonin in this system. L-DOPA, especially if administered with a peripheral DOPA decarboxylase inhibitor, blocked the caudate spindle. Although the transmitter was not identified identified, it was confirmed that L-DOPA (dopamine) decreases the excitability of the nigrostriatal system and suggests that the caudate spindle may be useful for the study of drugs in the treatment of Parkinsonism. (Author abstract modified)

182125 Funderburk, William H.; Johnson, David N.; Ward, John W. A. H. Robins Research Laboratories, Richmond, VA 23220 **Effects of dopaminergic stimulants on the caudate spindle.** Federation Proceedings. 32(3):247, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of dopaminergic stimulants in cats were reported. Dopamine receptor stimulation suggested for two other compounds: 7-(2'-pyrimidyl)-4-piperonyl-piperazine (ET-495) and 2(p-nitrobenzylthio)-2-imidazoline HCl (NBTI). Twenty-five mg/kg of apomorphine or 10mg/kg of amantadine promptly blocked the spindles without markedly altering the spontaneous cortical potentials. NBTI, in doses of 15mg/kg, also promptly blocked caudate spindling while the action of ET-495 was slower in onset. Following 20mg/kg of ET-495, peak effect was attained in 2 to 3 hours. To confirm these data, apomorphine (2mg/kg), NBTI (50 mg/kg), ET-495 (100 mg/kg), and amantadine (75mg/kg) were also studied in mice with unilateral caudate lesions. The first three drugs promptly produced homolateral body asymmetries and pivoting. Amantadine produced the same effects but required up to 1 hr for onset of action. It was concluded that drugs which block the caudate spindle may be useful in the treatment of Parkinsonism. (Author abstract modified)

182126 Schlosser, W.; Franco, S.; Zavatsky, E. Research Division, Hoffmann-LaRoche Inc., Nutley, NJ 07110 **A comparison of somatic reflex effects of three psychotropic agents in the chloralose cat.** Federation Proceedings. 32(3):247, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of diazepam, diphenylhydantoin (DPH) and phenobarbital on L7 ventral root discharge evoked by afferent stimulation were compared in the chloralose anesthetized cat. In this preparation, afferent stimulation produces an initial short latency spinal discharge (monosynaptic (MSP) and polysynaptic potentials) followed by a longer latency spino-bulbospinal reflex (SBS). Phenobarbital markedly depressed the MSP recorded following stimulation of extensor or flexor afferents by 74% and 88%, respectively. Diazepam was not as effective, reducing the MSP to about 72% of control. DPH initially enhanced this reflex slightly, followed by a depression of similar magnitude as observed with diazepam. Polysynaptic activity was depressed to the greatest extent by phenobarbital (to 36% of control) followed by DPH (46%) and diazepam (62%). The SBS reflex resulting from fore or hindlimb cutaneous afferent stimulation was blocked by phenobarbital and diazepam, but not by DPH. In fact, an initial enhancement was often seen with DPH after forelimb stimulation. (Author abstract)

182127 Seeman, P.; Staiman, A.; Chau-Wong, M. Pharmacology Department, University of Toronto, Toronto, Ontario, Canada **Neurone-blocking actions of anti-psychotic drugs.** Federation Proceedings. 32(3):248, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the hypothesis that antipsychotic drugs may act by anesthetizing selective regions within the brain was tested. The nerve blocking concentrations of neuroleptic drugs on nerves having neurons of different diameters was examined. The compound action potential of rat phrenic nerve was reduced by 50% at by trifluperidol, haloperidol, chlorpromazine, imipramine, promethazine and procaine HCl, 10% block occurred at values half those for 50% block, and 90% block occurred at values double those for 50% block. The frog sciatic nerve was blocked at values about 15 fold higher than those for rat phrenic nerve, while those for 10 C day old rat phrenic nerves were about two fold lower. The blocking concentration for each drug thus varies directly with the neurone average diameter. These findings support the neuron blockade theory of neuroleptic action since the clocking potencies correlate with clinical potency, and since the drugs can produce 10% block of fibers at concentrations found in patients' serum. Neuroleptic induced Parkinsonism may thus be due to nigral fiber block and not due to dopamine receptor blockade. (Author abstract)

182129 Baker, W. W.; Zivanovic, D. Department of Neuropharmacology, Eastern Pennsylvania Psychiatric Institute, Philadelphia, PA 19129 **Analysis of tremorgenic effects of intracaudate d-amphetamine.** Federation Proceedings. 32(3):248, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, an analysis of tremorgenic effects of intracaudate d-amphetamine was reported. Tremors of short duration developed in chronic cats within 10 minutes after intracaudate injection of small doses of d-amphetamine. Higher doses (30-300micrograms) increased the intensity and prolonged the tremor responses without producing concomitant electrical changes locally in the caudate or in projected cortical brain areas. Also, no evidence of tachyphylaxis to repeated challenging doses of amphetamine was demonstrated. These tremors were readily and reversibly suppressed by subsequent i.c. injections of dopamine or pargyline, but not by local hemicholinium-3 (180micrograms), scopolamine or methysergide. Small doses of chlorpromazine abolished amphetamine tremors which could then be reestablished only at substantially higher doses of amphetamine. Both physostigmine and serotonin, however, potentiated ongoing amphetamine tremor activity. Data suggest that dopamine, rather than endogenous acetylcholine or serotonin, is more directly involved in the tremorgenic effects of amphetamine; they also suggest that these tremors result primarily from an interference with local mechanisms which determine the stabilizing functions of dopamine, rather than serotonin, in the caudate. (Author abstract)

182130 Brezenoff, H. E.; Cohen, G. College of Medicine and Denistry of New Jersey, Newark, NJ **Hypothermia evoked by a dopamine-derived tetrahydroisoquinoline alkaloid.** Federation Proceedings. 32(3):248, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, hypothermia evoked by a dopamine derived tetrahydroisoquinoline alkaloid was reported. In the rat, intraventricular injection of 6,7-dihydroxytetrahydroisoquinoline (TIQ), a condensation product of dopamine and formaldehyde, was followed by a rapid, dose related hypothermia. Central administration of 6-hydroxydopamine reduced brain catecholamines to approximately 40% of control and caused a six fold reduction in the hypothermic effect of TIQ. Norepinephrine (N) also caused hypothermia; however, unlike TIQ, this response was not inhibited by 6-hydroxydopamine. These results suggest that TIQ causes hypothermia by releasing catecholamines from central adrenergic nerve terminals. In addition, when injected in doses below those eliciting hypothermia, N, but not TIQ, evoked a hyperthermic response. Since released catecholamines caused only hypothermia, these results suggest that central catecholamines mediate hypothermia and that the hyperthermia following low doses of N is a pharmacological rather than physiological response. (Author abstract modified)

182134 Webb, Roy W.; Tipton, Roderick K.; Maickel, Roger P. Department of Pharmacology, Medical Science Program, Indiana University, Bloomington, IN 47401 **Studies on the anorexigenic action of phentermine.** Federation Proceedings. 32(3):275, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the production of tolerance to the appetite depressant effects of alpha,alpha-dimethylphenylethylamine (phentermine) was reported. When administered to rats p.o. as a solution of the hydrochloride salt,

a decreased effect is seen over 6 days of dosage with phentermine. Subsequent 6 day dosage periods, interspersed with 6 day placebo periods show a dimunition of this apparent tolerance effect by the fourth drug period, while a 6 day drug 12 day placebo schedule continues to demonstrate tolerance for four drug periods. By contrast, when phentermine is administered p.o. as the resin-bound preparation no tolerance is seen in either the 6 drug 6 placebo or 6 drug 12 placebo schedules. The results suggest that tolerance to the effects of phentermine in this test system may be related to the pharmacokinetics of the drug in the body. (Author abstract modified)

182140 Gallager, D. W.; Sanders-Bush, E. Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, TN 37203 **In vivo measurement of the release of 5-hydroxytryptamine (5HT) from the hippocampus of the rat: effect of R04-1284, pargyline and p-chloroamphetamine (PCA).** Federation Proceedings. 32(3):303, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the use of the push - pull cannula technique to measure drug induced changes in the release and metabolism of 5-hydroxytryptamine (5HT) in brain was reported. After stereotaxic implantation of a push - pull cannula into the dorsal hippocampus of the rat, endogenous 5HT in brain was labeled by intraventricularly injected 3H-5HT. Spontaneous and drug induced release of 3H-5HT and its metabolite, 5-hydroxyindole acetic acid (5HIAA), into the perfusate were measured. In control animals, radioactivity in the perfusate decreased with time, but the ratio of 5HT/5HIAA remained constant. The well known releasing agent, R04-1284, increased the release of radioactivity into the perfusate, with 5HIAA accounting for most of the increase. Pargyline dramatically increased both the amount of total radioactivity in the perfusate and the ratio of 5HT/5HIAA. PCA caused a rapid increase in the release of total radioactivity into the perfusate with no significant change in the ratio of 5HT/5HIAA. The PCA induced release of 5HT was not blocked by pretreatment with 6-hydroxydopamine, suggesting that this effect is not mediated through noradrenergic mechanisms. (Author abstract)

182141 Haigler, H. J.; Aghajanian, G. K. Department of Pharmacology, Yale University School of Medicine, New Haven, CT 06519 **A comparison of effects of D-lysergic acid diethylamide (LSD) and serotonin on pre- and postsynaptic cells in the serotonin system.** Federation Proceedings. 32(3):303, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, a comparison of effects of d-lysergic acid diethylamide (LSD) and serotonin on presynaptic and postsynaptic cells in the serotonin system was reported. LSD inhibits the firing of serotonin (5HT) containing neurons in the midbrain raphe nuclei of rats when it is administered in small amounts either directly (by microiontophoresis) or intravenously. 5HT applied microiontophoretically at low ejection currents to these presynaptic cells is also inhibitory. Postsynaptic areas include the cortical nucleus of the amygdala, the ventral lateral geniculate, and the ventral hippocampus. When 5HT was administered microiontophoretically to cells in these areas, inhibition of firing was usually produced at the same low ejection currents that were effective in raphe cells. However, microiontophoretic LSD did not inhibit the postsynaptic cells except at ejection current levels much higher than required for the presynaptic cells, nor did it block the inhibition produced by 5HT. Intravenous LSD consistently inhibited raphe cells, but this same low dose often produced an acceleration in the discharge rate of the postsynaptic cells. This acceleration may be due to a release from a tonic inhibitory influence of the raphe on the postsynaptic cells, suggesting that LSD in low doses primarily has a presynaptic action in the 5HT system. (Author abstract)

182143 Huang, Chuong C.; Marrazzi, Amedeo S. University of Missouri Institute of Psychiatry, St. Louis, MO 63139 **Analysis of drug block of LSD/5HT/GABA by monitoring neuronal membrane changes.** Federation Proceedings. 32(3):303, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, an analysis of drug block by lysergic acid diethylamide (LSD), serotonin (5-HT), and gamma-aminobutyric acid (GABA) in cats was reported. Continuous intracellular monitoring of membrane changes in pyramidal, pericruciate cortex cells establishes that close arterially injected 5HT, LSD and chlorpromazine (CPZ) act in a qualitatively identical fashion, with 5HT being most active, LSD less, and CPZ very much less. In all three the concomitant changes are: reduced or stopped firing, hyperpolarization, reduced EPSPs, appearance and increase of IPSPs, and decreased

conductance. Thus, CPZ appears to block by substituting at, evidently, the identical membrane site on identical but much weaker action for 5HT or LSD, demonstrating competitive inhibition in terms of critical membrane changes. CPZ local anesthesia is excluded as a factor since xylocaine, enough to reduce firing, did not reproduce the other changes. GABA membrane changes are similar except for an increased conductance. Strychnine (Strych) blocking all, is less specific and blocks GABA, presumably, largely by reducing inhibition in another contributing channel rather than the high conductance one. The data provide a cellular basis for a specific, competitive, and differential inhibition (CPZ), and for a less specific block (Strych.). (Author abstract)

182150 Locke, Steven; Dembiec, Dorothy; Cohen, Gerald. Mount Zion Hospital, San Francisco, CA **In vivo inhibition of neuronal uptake of a dopamine-derived tetrahydroisoquinoline (TIQ) alkaloid by cocaine and by desmethylimipramine (DMI).** Federation Proceedings. 32(3):526, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the in vivo inhibition on neuronal uptake of a dopamine derived tetrahydroisoquinoline (TIQ) alkaloid by cocaine and by desmethylimipramine (DMI) was reported. When injected iv into mice and rats this alkaloid accumulated in sympathetically innervated tissues such as the heart, iris and salivary glands. That a major fraction of the uptake of the H3-alkaloid was due to accumlation by adrenergic nerve terminals was evident by comparison of normal tissues to hearts of chemically denervated mice (6-hydroxydopamine treated) and to irides and submaxillary glands of surgically denervated rats (unilateral superior cervical ganglionectomy). In experiments with mice, it was found that cocaine and DMI, two well known inhibitors of the axonal membrane pump for norepinephrine, each diminished the accumulation of H3-6,7-dihydroxy-TIQ into the heart by 50-75%. The results may have relevance to an understanding of altered adrenergic function during ingestion of alcohol. (Author abstract modified)

182153 Patrick, G. A.; Harris, L. S. University of North Carolina, Chapel Hill, NC 27514 **Effects of selected centrally acting agents on adenyl cyclase activity in mouse brain.** Federation Proceedings. 32(3):679, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of selected centrally acting agents on adenyl cyclase activity in mouse brain were reported. Adenyl cyclase activity was assayed in mouse brain homogenates by the Ba-Zn precipitation method. Toth basal and fluoride stimulated enzyme activities were measured, and the in vitro effects of a number of centrally acting drugs on these activities were studied. Morphine sulfate, naloxone, pentobarbital, d-amphetamine, and chlordiazepoxide showed little or no effect on enzyme activity. Phenothiazine tranquilizers, tricyclic antidepressants, and certain synthetic tetrahydrocannabinol analogues did produce significant effects. The tricyclic drugs exhibit both stimulatory and inhibitory effects on the enzyme, with stimulation occurring at lower concentrations and inhibition at higher concentrations. In vivo tests were also performed to determine the effects of these centrally acting drugs on the adenyl cyclase cyclic AMP system in the intact animal. Responses were largely negative at doses of the drugs which produced pharmacologic effects. (Author abstract modified)

182154 Kimura, H.; Thomas, E.; Murad, F. University of Virginia, Charlottesville, VA 22903 **Effects of decapitation, ether and pentobarbital on cyclic AMP and cyclic GMP levels in rat tissues.** Federation Proceedings. 32(3):680, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of decapitation, ether and pentobarbital on cyclic AMP and cyclic GMP levels in rat tissues were reported. Cyclic AMP and cyclic GMP were determined in various rat tissues after animals were immersed in liquid nitrogen (LN) or decapitated (D) and after anesthesia with ether (E) or pentobarbital (P). Cyclic AMP levels were 2-15 fold higher in cerebral cortex, cerebellum and liver after D or E compared to animals immersed in LN. Cyclic GMP levels of cerebral cortex and liver were not changed by D or E, while cyclic GMP in cerebellum increased two fold. Lung, heart, kidney and testis cyclic AMP levels were unchanged or minimally altered to D and E, while cyclic GMP levels increased in all except kidney. There was no change in cyclic GMP levels in some tissues that had increased or decreased cyclic AMP levels by some treatments, and vice versa. These observations indicate that synthesis and/or degradation of these nucleotides in tissues are regulated differently and not necessarily in a parallel or reciprocal manner. (Author abstract modified)

182155 Cohn, M. L.; Kraynack, B.; Cohn, M.; Scattaregia, F. University of Pittsburgh, Pittsburgh, PA 15213 **Interaction of cyclic AMP with neuropharmacologic depressant agents.** Federation Proceedings. 32(3):680, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the interaction of db cyclic AMP (db cAMP) with neuropharmacologic depressant agents was reported. Dibutyryl surrogate of cyclic AMP administered intracerebroventricularly (ICV) regulated in a dose related manner the duration of amobarbital induced narcosis. Structurally different neuropharmacologic depressant agents (the aliphatic hypnotics, chloral hydrate and paraldehyde, the tranquilizer, diazepam, the phencyclidine derivative, ketamine, and the inhalation agent, halothane) were similarly antagonized. Sprague-Dawley male rats weighing 80-125 g were given intraperitoneal injections of one of the CNS depressant agents: ethanol; methanol; meperidine; lidocaine. Each rat was given an ICV injection of db cAMP in varying concentrations. Ethanol and methanol sleeping time and overdosage were antagnozied in a manner similar to those produced by amobarbital. In contrast, the ICV administration of db cAMP to meperidine and lidocaine treated rats augmented the toxic effects and increased the mortality. The data suggests that there are two general groups of neuropharmacologic CNS depressant agents. They may be classified according to their response to exogenously administered db cAMP. (Author abstract)

182156 Mark, Lester C.; Brand, Leonard; Heiber, Sofia; Smith, Doris; Carroll, F. Ivy. Department of Anesthesiology, Columbia University, New York, NY **Pharmacologic activity and biotransformation of R+ and S- barbiturate enantiomers in mouse and man.** Federation Proceedings. 32(3):681, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the pharmacologic activity and biotransformation of R+ and S- barbiturate enantiomers in mouse and man were reported. Optically pure R+ and S- enantiomers of pentobarbital, thiopental and thiamylal, each labeled at the 2-14C position, were synthesized de novo. After pentobarbital isomers, in mice, time to peak action and total sleep time were both significantly longer with the S- form. Opposite effects were observed with optically pure R+ and S- enantiomers of thiopental given separately at intervals of 2-4 weeks to three human volunteers in doses of 300mg. Durations of sleep and apnea were consistently longer with the R+ isomer. Responses to the antipodes of thiamylal did not differ significantly in any one subject despite considerable variability from one subject to another, a fact which emphasizes the importance of using each subject as his own control. Plasma decay curves and urinary excretion patterns of the thiobarbiturate isomers were compared in man. With thiamylal, T 1/2 was identical with the R+ and S- isomers in the same subject, while with thiopental both T 1/2 and plasma levels were greater with the R+ than the S- isomer. (Author abstract)

182157 Tabakoff, B.; Vugrincic, C.; Anderson, R.; Delneky, P. Department of Biochemistry, Chicago Medical School, Chicago, IL 60612 **Conversion of chloral hydrate to trichloroethanol in brain and liver.** Federation Proceedings. 32(3):683, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the conversion of chloral hydrate (CH) to trichloroethanol (TCE) in brain and liver was reported. The enzyme activity from rat brain was compared to the activity found in the liver cytosol. The metabolism of CH in brain cytosol was shown to be dependent on NADPH, while the liver enzyme utilized either NADH or NADPH. The production of TCE by the brain enzyme was shown to be stoichiometric with the utilization of 1 mole of NADPH per mole of TCE formed. The brain and liver enzymes were differentiated by their ability to metabolize ethanol, propionaldehyde, and aromatic aldehydes, as well as CH. The metabolism of CH by the brain enzyme was not affected by pyrazole, while pyrazole strongly inhibited CH metabolism by the liver enzyme. Pentobarbital inhibited CH metabolism by both brain and liver enzymes. These studies suggest that CH is metabolized in brain by an aldehyde reductase, while in liver both the classic alcohol dehydrogenase, as well as aldehyde reductase, might participate in CH metabolism. (Author abstract modified)

182158 Karbowski, Michael J. Department of Pharmacology, University of Michigan Medical School, Ann Arbor, MI 48104 **Lack of effects of cycloheximide on tolerance development to a stimulatory effect of morphine on mice.** Federation Proceedings. 32(3):687, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of protein synthesis inhibition on the development of tolerance to a stimulant effect (mouse locomotor activity) were reported. Mice were given concurrent injections of morphine and cycloheximide. Tolerance was assessed by measuring locomotor activity in double photocell chambers following 1,2,4,6 and 8 injections of morphine plus cycloheximide. In addition, the number of jumps induced by naloxone were recorded since many authors have used this procedure to assess the degree of physical dependence. At all doses, cycloheximide did not affect either the degree or rate of tolerance development, nor did it reduce the amount of naloxone induced jumping. (Author abstract modified).

182159 Bhargava, Hemendra N.; Afifi, A. H.; Way, E. Leong; Cullen, S. C. Pharmacology Department, University of California, San Francisco, CA 94122 **Effect of chemical sympathectomy on morphine antinociception and tolerance in rats.** Federation Proceedings. 32(3):687, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the role of catecholamines in morphine antinociception and tolerance was reported. The effect of intraventricular administration of 6-hydroxydopamine (6-OHDA) in nontolerant and tolerant rats was compared. Prior to rendering the rats tolerant to morphine by pellet implantation, 6-OHDA was injected either at dose of 1.3mg/kg or 0.5mg/kg daily for two consecutive days. Thirty six hours after the first implant, both groups were implanted with a second pellet and after an additional 36 hrs the pellets were removed. Six hrs later, the analgetic dose of morphine was determined in tolerant animals and compared with the morphine AD5O obtained in the same animals before pellet implantation. Both dosage regimens of 6-OHDA caused dose dependent reduction in brain norepinephrine and dopamine and antagonized morphine antinociception as evidenced by an increase in the morphine AD50; however, the development of tolerance was not affected. (Author abstract modified).

182160 Castles, T. R.; Bristow, R. L.; Hodgson, J. R. Midwest Research Institute, Kansas City, MO 64110 **Chromatin template activity during morphine-induced analgesia and the development of analgesic tolerance.** Federation Proceedings. 32(3):687, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the template activity of brain chromatin isolated from saline treated rats was compared to the template activity in morphine induced analgesia and at various times during the development of analgesic tolerance. During analgesia produced by a single subcutaneous injection of morphine sulfate, chromatin template activity was unchanged. When analgesic tolerance was produced by gradually increasing morphine dosage from 10 to 100mg/kg/day over 13 days, gradual decreases in chromatin template activity occurred. These decreases were 7%, 16%, 23%, and 30% for 1, 3, 6, and 13 days, respectively. The depression of chromatin template activity and analgesic tolerance were both significant by the 3rd day. These data are consistent with the possibility that RNA transcription is linked to the development of morphine induced analgesic tolerance. (Author abstract modified).

182161 Schulz, Rudiger; Goldstein, Avram. Addiction Research Laboratory, Department of Pharmacology, Stanford University, Stanford, CA 94305 **The effect of catecholamines, acetylcholine and serotonin on the morphine tolerant longitudinal muscle strip of the guinea pig ileum.** Federation Proceedings. 32(3):688, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effect of catecholamines, acetylcholine and serotonin on the morphine tolerant longitudinal muscle strip of the guinea pig ileum was reported. Electrically stimulated morphine tolerant muscle strips display reduced sensitivity to catecholamines. The required epinephrine concentration for a 50% twitch inhibition is about five times higher than in controls. The dose response curve observed for isoproterenol showed a similar shift to the right, producing a maximal depression of only 30%. The greatest loss of sensitivity was seen for dopamine. The ED50 in controls required a concentration of 5.8x 10 sup-6 M, but in the morphine tolerant state the maximal depression was only about 25%. The response of the unstimulated strip to acetylcholine was not different in controls or tolerant preparations. On the other hand, the tolerant strip exhibits a 10 times higher sensitivity to serotonin. Naloxone did not block or reverse the effects of the test compounds. The supersensitivity to serotonin could be caused by a feedback mechanism in the excitatory pathway of the myenteric plexus, and it could account for the

morphine tolerance. In this system, a catecholamine may act as an inhibitory modulator of neurotransmission. (Author abstract).

182162 Villarreal, J. E.; Dummer, G. E. Department of Pharmacology, University of Michigan Medical School, Ann Arbor, MI 48104 **Separation of the dependence-producing actions from the direct actions of narcotics on guinea pig ileum.** Federation Proceedings. 32(3):688, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the separation of the dependence producing actions from the direct actions of narcotics on guinea pig ileum was reported. At low concentrations, naloxone reverses the depressant effect of narcotics on the electrically elicited twitch of the guinea pig ileum. In addition, at high concentrations naloxone produces transient contractions in untreated ilea. The latter effect of naloxone is markedly potentiated by chronic in vivo treatment with either morphine or levorphanol; six to 33 fold to the left and its maximum is three times higher. By analogy with findings in intact organisms this sensitization to naloxone contractions is evidence of narcotic dependence. Like morphine, nalorphine has direct depressant effects on the ileum. However, chronic in vivo treatment with nalorphine does not sensitize the ileum to naloxone. Therefore, the sensitization to naloxone induced contractions does not appear to be a secondary result of the direct (type I) depressant effects of narcotics but of some other actions (type II) present in morphine and not present in nalorphine. (Author abstract modified)

182163 Nutt, J. G.; Jasinski, D. R. NIMH Addiction Research Center, Lexington, KY 40507 **Comparison of intravenously administered methadone (ME), morphine (MO), heroin (H) and placebo (P).** Federation Proceedings. 32(3):694, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, a comparison of intravenously administered methadone (Me), morphine (Mo), heroin (H) and placebo (P) was reported. Me, Mo, H and P were administered i.v. to 10 subjects to compare their relative abilities to produce subjective effects and miosis. Drugs were administered double blind at weekly intervals in random order. Pupil changes were assessed photographically at these same times. Me, as well as H and Mo, produced dose related miosis and increases in scale scores measuring Mo like effects. On measures of subjective effects Me, Mo and H showed similar time action curves with marked decrements in scale scores for subjective effects at 12 and 24 hrs. On pupils, H and Mo showed decrements in miosis at 12 and 24 hrs; however, Me produced miosis which was sustained near maximum at 12 and 24 hrs. Me was equipotent to Mo and H was twice as potent as Mo in producing miosis and Mo like subjective effects and euphoria. Subjects did not specifically identify or distinguish Me from Mo and H. It is concluded that Me produces typical Mo like euphoria and subjective effects with a relative potency to morphine similar to the potency for producing miosis and relief of pathological pain. (Author abstract modified)

182164 Smith, A. A.; Hui, F. W.; Crofford, M. Department of Anesthesiology, New York Medical College, New York, NY 10029 **Inhibition of growth in animals treated with methadone.** Federation Proceedings. 32(3):694, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the inhibition of growth in animals treated with methadone was reported. Injection of the salamander with methadone, 2mg/kg or with levorphanol, 10mg/kg prevented regeneration of the amputated hind limb. Blastema failed to develop despite formation of a thick epidermal cap at the wound site. The antagonist, levallorphan, 10mg/kg, which also possesses agonistic activity, initially blocked blastemal development for 4 weeks but then normal growth began. Phalanges appeared 4 weeks later than control. Naloxone, the pure antagonist, neither altered blastemal development nor prevented normal regeneration and differentiation. Treatment with the opioids methadone or levorphanol produced some atrophy of the lingual epithelium and of the taste buds of the salamander. Atrophy of taste buds suggests a peripheral action for opioids. Newborn mice treated daily with methadone, 2mg/kg to 4mg/kg for up to 6 weeks, grew far more slowly than did saline treated littermates. Naloxone treatment prevented growth inhibition. The adverse effects on growth of cholinolytic drugs in salamanders suggest that the action of methadone in retarding growth of mice may be related to the ability of this opioid to inhibit the release of acetylcholine. (Author abstract modified)

182165 Peters, Marvin A. Loma Linda University, Loma Linda, CA 92354 **The development of a**

blood-brain barrier to methadone in the newborn rat. Federation Proceedings. 32(3):694, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the development of a blood - brain barrier to methadone in the newborn rat was examined. It is suggested that at some time following birth and prior to adulthood a partial barrier to the passage of methadone into the central nervous system must develop. At about 25 to 30 days following birth the young rats, from control mothers, develop a mechanism by which methadone passage into the brain is reduced and the young animals begin to respond more like adult animals in regard to the distribution of methadone into the brain. Preliminary evidence suggests that such a barrier may develop somewhat slower in infant rats whose mothers are treated daily with methadone. It appears that if the distribution of methadone in fetal and newborn rats is similar to the distribution of methadone and other drugs in human infants, drugs which normally never penetrate the CNS or enter the CNS in small amounts may have a profound effect on the CNS of the newborn infant. (Author abstract modified)

182167 Boggan, William O.; Freedman, Daniel X. Department of Psychiatry, University of Chicago, Chicago, IL 60637 **LSD tolerance and brain serotonin metabolism.** Federation Proceedings. 32(3):694, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects on brain serotonin (5-HT) metabolism of LSD-25 administered on tolerance dosage schedules in rats were reported. Male Sprague Dawley rats were given either 7 injections of saline one/day for 7 days; 6 injections of saline and one injection of LSD (L x 1); or 7 injections of LSD (L x 7). As compared to the L x 1 group, the L x 7 group manifested: 1) a shift to the left in the time course of serotonin elevation; 2) a significant reduction in the amount of 5-hydroxyindoleacetic acid depletion; and 3) control levels of brain tryptophan at time points (45, 60 and 75 minutes) when the single dose of LSD caused significant elevation. Whether the changes observed in 5-HT metabolism after one injection of LSD are a consequence of the reported decrease in synthesis of labeled 5-HT from labeled tryptophan after LSD, diminished neuronal activity, or alteration of uptake processes is unknown. (Author abstract modified)

182168 Halaris, A. E.; Lovell, R. A. Department of Psychiatry, Pritzker School of Medicine, University of Chicago, Chicago, IL 60637 **On the nature of the serotonin binding after LSD.** Federation Proceedings. 32(3):694, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, a study of the nature of serotonin (5-HT) binding was reported. It was concluded that the enhanced binding of 5-HT after LSD most probably occurs in the synaptic vesicles. To test this concept, animals were pretreated with reserpine. LSD was administered at 12, 22 and 48 hours after reserpine. LSD failed to cause an increase in 5-HT either in whole brain or in any subcellular fraction, provided that the animals were fully reserpinized. However, it did cause a significant decrease in the elevation of 5-hydroxyindoleacetic acid, which occurs after reserpine alone. These data are interpreted as indicating that the effect of LSD on 5-HT is contingent upon the availability of intact vesicles and that these organelles are the binding site of 5-HT. (Author abstract modified)

182170 Hrdina, Pavel D.; Ling, George M. Department of Pharmacology, University of Ottawa, Ottawa, Canada K1N 6N5 **Inhibition of C14-ACh uptake in rat brain slices by desmethylimipramine.** Federation Proceedings. 32(3):695, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effect of desmethylimipramine (DMI) on the accumulation of C14-acetylcholine (ACh) by rat cerebral cortex slices incubated in the presence of a cholinesterase inhibitor Sarin was reported. The analysis of kinetics of C14-ACh accumulation revealed that the uptake occurs against the concentration gradient and is inversely proportional to the concentration of ACh in the incubation medium. DMI inhibited the accumulation of labeled ACh by brain slices and this effect was dependent on the concentration of the drug in the medium. Graphic analysis using the Lineweaver-Burk plot indicated that the inhibition of ACh uptake by DMI is of a competitive type. It is suggested that the inhibitory effect of DMI on C14-ACh accumulation may be related to the ability of this drug to alter acetylcholine levels in certain brain areas. (Author abstract)

182171 Faragalla, F. F. Division of Research, North Carolina Department of Mental Health, Raleigh, NC 27611 **Brain amines in pyridoxine deficient rats.** Federation Proceedings. 32(3):696, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, a study of brain amines in pyridoxine deficient rats was reported. Twelve male weanling rats were fed vitamin B6 deficient diet and twelve other rats served as pair fed controls. The rats were sacrificed by decapitation after 14, 20 and 25 days on the diets. Serotonin (5-HT), dopamine (DA) and norepinephrine (NE) were assayed fluorometrically. After 2 weeks on the diets the levels of brain 5-HT, DA and NE in the vitamin B6 deficient animals were much lower than those in the controls, but the difference was not statistically significant. After days on the diets significant decrease in the levels of brain 5-HT and of DA was noted in the vitamin B6 deficient rats. After 25 days on the diets the brain levels of 5-HT, DA and NE in the vitamin B6 deficient rats were significantly less than those of the controls. These results indicate that brain amines are affected by dietary vitamin B6, and that brain 5-HT and DA were affected to the same extent. (Author abstract modified)

182184 Tobin, T.; Akera, T.; Baskin, S. I.; Brody, T. M. Department of Pharmacology, Michigan State University, East Lansing, MI 48823 **(3H) Ouabain binding to Na+ + K+-ATPase: inhibition by beta, gamma-methylene ATP.** Federation Proceedings. 32(3):709, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the inhibition of (3H) ouabain binding to Na+ + K+-ATPase by beta, gamma-methylene ATP (MeATP) was reported. This inhibition was apparently synergistic with that of Na+ because minimally inhibitory concentrations of Na+ potentiated the inhibition of (3H) ouabain binding by MeATP. This inhibitory action of MeATP was antagonized by the presence of Pi in the (3H) ouabain binding system. In other experiments the effects of ATP and MeATP on (3H) ouabain binding occurring in the presence of Na+, Mg++ and Pi were compared. Under these conditions ATP produced a prompt increase in (3H) ouabain binding, whereas MeATP completely inhibited (3H) ouabain binding within 10 minutes. The data show that nucleotide binding to the enzyme is not sufficient to support (3H) ouabain binding. (Author abstract modified)

182185 Yamaki, T.; Baez, S.; Gootman, P. M.; Feldman, S. M.; Orkin, L. R. Department of Anesthesiology, Albert Einstein College of Medicine, Bronx, NY **Microvascular smooth muscle hyperresponsiveness during halothane anesthesia in the rat.** Federation Proceedings. 32(3):714, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the mechanism of microvascular hyperresponsiveness during halothane anesthesia in the rat was examined. Halothane suppressed the depressor phase but not the peripheral hypersensitization to NE. Thus, although halothane decreases the microvascular response to CNS stimuli, the response to topical NE was enhanced. This suggests that microvascular hypersensitivity is a peripheral action of halothane or that the CNS dampening effect is decreased. (Author abstract modified)

182186 Schnoll, S. H.; Vogel, W. H.; Odstrchel, G. Thomas Jefferson University, Philadelphia, PA 19107 **The specificity of anti-mescaline antibody produced in rabbits.** Federation Proceedings. 32(3):719, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the specificity of antimescaline antibody produced in rabbits was reported. The specificity of the antibody was determined by a radioimmunoassay which employed possible cross reacting compounds. Cross reactivity was present with a methoxy group in the meta position and increased with additional methoxy groups on the aromatic ring. However, there was no cross reactivity when the ring was saturated with methoxy groups. Modification of the free amino group with a methyl or acetyl group gave increased cross reactivity. Using various catecholamines, serotonin, LSD, tryptamine, DMT and DET, a large molar excess was required to inhibit the mescaline antimescaline reaction. The antimescaline antibody offers a possible sensitive technique for the direct measurement of mescaline in body tissues and fluids. (Author abstract modified)

182187 Ringle, D. A.; Herndon, B. L. Midwest Research Institute, 425 Volker Blvd., Kansas City, MO 64110 **Binding of morphine by serum proteins of morphine-treated rabbits.** Federation Proceedings. 32(3):719, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the binding of morphine by serum proteins of morphine treated rabbits was reported. The possibility

that some aspects of tolerance to morphine are immunologic in nature was discussed. Results demonstrated an increase in morphine binding by sera following morphine treatment, with degree of binding related both to length of pretreatment and to method of dosage. Dosage by chronic s.c. pellet implantation of morphine free base was more effective than daily s.c. morphine sulfate injections. Preliminary findings indicated that the increased binding is associated with the globulin fractions prepared by ammonium sulfate precipitation. The results of these studies suggest that rabbits are capable of responding immunologically to morphine through the production of an immunoglobulin directed against the morphine configuration. (Author abstract modified)

182204 Mytilineou, Catherine; Cohen, Gerald; Barrett, Robert. Columbia University Medical School, New York, NY **Uptake, storage & release in vivo of a dopamine-derived tetrahydroisoquinoline (TIQ) alkaloid by sympathetic nerves of the iris.** Federation Proceedings. 32(3):739, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the uptake, storage and release in vivo of a dopamine derived tetrahydroisoquinoline (TIQ) alkaloid by sympathetic nerves of the iris was reported. Mice received reserpine to deplete endogenous norepinephrine (NE) from sympathetic nerves. Irides removed 5-60 minutes later showed a brightly fluorescent nerve plexus with prominent varicosities (nerve terminals). Control mice did not exhibit fluorescence. These results demonstrate uptake and storage in vivo of the TIQ alkaloid by sympathetic nerves. Rats were pretreated with alpha-methyl-p-tyrosine (to deplete endogenous NE) and they received 6,7-dihydroxy-TIQ by iv injection. The preganglionic fiber of one superior cervical ganglion was stimulated for 30 min (6 V, 2 msec.,15 per sec). Comparison of experimental and control irides revealed that stimulation depleted the TIQ from the nerve terminals. Thus, this TIQ alkaloid was taken up and stored by sympathetic nerve terminals in vivo and it was secreted upon preganglionic stimulation. Results support a false transmitter role for endogenously formed TIQ alkaloids during ingestion of alcoholic beverages. (Author abstract modified)

04 MECHANISM OF ACTION: BEHAVIORAL

175242 Rosen, Alexander J.; La Flore, Johnny E. University of Illinois at Chicago Circle, Chicago, IL **Effects of intraperitoneal and intraventricular d-amphetamine administration on active avoidance performance in the rat.** Life Sciences (Oxford). 13(11):1573-1580, 1973.

The effects of intraventricular and intraperitoneal administration of d-amphetamine on active avoidance performance were examined in the rat. Intraventricular and intraperitoneal administration of d-amphetamine impaired asymptotic shuttlebox avoidance performance in rats. Low doses had no effect whereas higher ip doses impaired performance in a dose related fashion. An inverted U-shaped function was obtained with the iv doses; low dose and high doses impaired performance whereas intermediate doses had little effect. The cannulation procedure itself produced only minimal acquisition effects. The data tend to support the contention that amphetamine acts on the brain to cause the deterioration of well learned avoidance responding. 15 references. (Author abstract)

175317 Miller, Robert E.; Levine, John M.; Mirsky, I. Arthur. Department of Psychiatry, 3811 O'Hara Street, Pittsburgh, PA 15213 **Effects of psychoactive drugs on nonverbal communication and group social behavior of monkeys.** Journal of Personality and Social Psychology. 28(3):396-405, 1973.

The effects of psychoactive drugs on nonverbal communication and group social behavior of monkeys were studied. In comparison with nontreated conditions, the stimulant improved communications in cooperative conditioning, the tranquilizer markedly damped both transmission and reception of nonverbal cues, and the hallucinogen only slightly affected transmission and reception. Findings indicate that the stimulant facilitated intergroup social behavior and reduced agression, the tranquilizer reduced the attractiveness of the treated animal to its untreated partners, and the hallucinogen drastically reduced all social behavior within the group and markedly augmented the proportion of aggressive responses directed toward the drugged subject. An inverse relationship between transmission ability and receptive sensitivity was found in untreated subjects, a finding which has also been reported for human subjects. 21 references. (Author abstract modified)

175877 Kamano, Dennis K. Galesburg State Research Hospital, Galesburg, IL 61401 **Effects of stimulus associated with amobarbital administra-**

tion on avoidance behavior. Physiological Psychology. 1(4):321u323, 1973.

The effect of avoidance of superimposing a stimulus which has previously been associated with amobarbital administration was evaluated. Rats were given unsignaled shuttlebox avoidance training, then given separate Pavlovian conditioning (conditioned stimulus (CS) and amobarbital pairings), with avoidance training continuing on alternate days. The Pavlovian CS was then presented during two test sessions to determine its effects on the avoidance response. It was found that the Pavlovian CS, through its association with amobarbital, suppressed the avoidance response rate when presented during nonsignaled avoidance behavior. 11 references. (Journal abstract modified)

175884 Jarbe, Torbjorn U. C.; Henriksson, Bengt G. Dept. of Psychology, University of Uppsala, Slottsgrand 3, S-752 20 Uppsala, Sweden **Vocalization: a characteristic cannabis-induced behavior in the rat?** Physiological Psychology. 1(4):351-353, 1973.

The effects of some psychotropic drugs on the tetrahydrocannabinol (THC) induced vocalization behavior in rats were studied. It was found that tranquilizers, morphine, and tacrine inhibited THC induced vocalization. Phenitrone was found ineffective in this respect. Vocalization was not noted after injection with two other naturally occuring cannabinoids, cannabinol and cannabidiol. The possibility that THC has aversive properties in rats is discussed. 24 references. (Journal abstract modified)

176861 Geller, Irving; Hartmann, Roy. Southwest Foundation for Research and Education, San Antonio, TX 78284 **Attenuation of 'conflict' behavior with cinanserin (2'-(3-dimethylaminopropylthio) cinnamanilide hydrochloride), a serotonin antagonist: reversal of the effect with 5-hydroxytryptophan (5-HTP) and alpha-methyltryptamine.** Federation Proceedings. 32(3):817, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, cinanserin, a serotonin antagonist reported to work through receptor blockade, was evaluated for its effect on conflict behavior of laboratory rats. The conflict was induced by punishing with electic shock, lever responses made in the presence of a tone stimulus. This procedure produced a suppression of lever pressing during tone periods. Cinanserin, given one hour prior to an experimental session, reinstated the suppressed behavior. Alpha-methyltryptamine and 5-HTP, given respectively 30 minutes or 25 minutes after cinanserin, lessened the attenuating action of the serotonin antagonist. These data further suggest the possible involvement of the brain serotonergic system in behavioral suppression and in the action of minor tranquilizers. (Author abstract modified)

176863 Yen-Koo, H. C. Y.; Davis, Dowell A. Division of Drug Biology, Bureau of Drugs, FDA, HEW, Washington, DC 20204 **Protection produced by benzodiazepines (BDP) against the neurotoxic and conflict-behavior effects of hexachlorophene (HCP) in cats.** Federation Proceedings. 32(3):817, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the protection produced by benzodiazepines (BDP) against the neurotoxic and conflict behavior effects of hexachlorophene (HCP) in cats was reported. HCP produced a disruption of conditioned response (CR) and caused vocalization, Straub tail, leg muscle stiffness, impaired gait, loss of appetite and weight, and dehydration. However, if cats were dosed with BDP 1 hour prior to HCP, the clinical signs of neurotoxic effects were diminished or abolished. This interaction of BDP with HCP is similar to BDP reversed conflict behavior facilitated by caffeine and d-amphetamine thus; a pharmacologic action rather than a pharmacokinetic mechanism is considered as the basis of the BDP effects. (Author abstract modified)

176864 Nelsen, Judith M.; Goldstein, Leonide. Rutgers Medical School, Piscataway, NJ 08854 **Acquisition and performance of an attention task by rats subjected to chronic nicotine treatment.** Federation Proceedings. 32(3):817, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the acquistion and performance of an attention task by task by rats subjected to chronic nitcotine treatment were examined. Rats were required to make a single lever press for food following a short, variably presented stimulus light and, also, to inhibit inappropriate responses. Nicotine impaired acquisition of the task as indicated by poorer correct responding and and greater intersession variability (compared to the behavior of saline treated rats). However, during the two

postacquistition performance phases, rats performed more efficiently with nicotine treatment than with saline, independent of the condition under which the task was learned and independent of whether they received nicotine during the earlier or later performance phase. Nicotine related improvement was evidenced by reductions in inappropriate responding. The results support the suggestion that one functional consequence of chronic nicotine treatment is the enchancement of incentive related behavior. (Author abstract modified)

176866 Oglesby, Michael W.; Winter, J. C. Department of Pharmacology, SUNY, Buffalo, NY 14214 **Post-trial strychnine: lack of effect on conditioned avoidance learning.** Federation Proceedings. 32(3):818, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, facilitation of learning by posttrial injection of strychnine sulfate was reported. Eight different doses of strychnine were employed, ranging from 0.005 to 0.60mg/kg. Groups treated with strychnine did not differ significantly from control in any of the five experiments. Because the control groups did not differ significantly among themselves, data from all experiments were combined. Using the mean number of avoidances over all sessions, a one-way analysis of variance showed no significant differences between any of the treatment conditions, nor was there concomitant variation in the dose effect relationship. These results do not support the conclusion that strychnine facilitates learning. (Author abstract modified)

176868 Radcliffe, G. J., Jr.; Shelton, J. W. Baylor College of Medicine, Houston, TX 77025 **Specific facilitation of maze learning by a peptide extracted from trained mouse brain.** Federation Proceedings. 32(3):818, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the specific facilitation of maze learning by a peptide extracted from trained mouse brain was reported. Water deprived mice were trained in complex mazes with water reward. After reaching criterion they were killed and their brains were removed, homogenized, extracted with water and centrifuged. The supernatant was injected into water deprived naive mice (500mg donor brain per recipient). These were found to run the maze significantly faster than the controls injected with untrained brain extract. In other experiments, donors were trained in two different mazes. Recipients tested in the same maze in which their donors were trained learned significantly faster than those that were tested in the other maze. The latter were not significantly different from the controls. The results indicate a surprisingly high degree of specificity of the information transferred from donors to recipients. (Author abstract modified)

176869 Marquis, W. J.; Tilson, H. A.; Rech, R. H. Michigan State University, East Lansing, MI 48823 **Effects of amphetamine (A), LSD, psilocybin (P), and DOM on schedule-controlled behavior in the rat.** Federation Proceedings. 32(3):818, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of amphetamine (A), LSD, psilocybin (P), and DOM on schedule controlled behavior in the rat were reported. A produced a dose dependent increase in DRL responding with an associated loss of reinforcers and shortening of IRTs. DOM produced an amphetamine like effect on DRL responding, whereas P and LSD produced no consistent behavioral effects. Higher doses of P, DOM, and LSD tended to decrease DRL responding. In the Sidman avoidance (SA) schedule, A and most doses of DOM increased responding with an associated loss of shocks and a shortening of IRTs. Low to moderate doses of P and LSD tended to decrease the number of shocks received without increasing the rate of SA responding. Higher doses of P and LSD tended to decrease SA responding, while increasing IRTs and the number of shocks. These data suggest that, within the dose range investigated, psychotomimetic drugs with an indolealkylamine structure differ in their mechanism of action from DOM. (Author abstract modified)

176873 Geller, Irving; Hartmann, Roy J.; Croy, Dan J.; Haber, Bernard. Division of Psychopharmacology, Department of Psychiatry, Texas Tech University Sch. of Med., Lubbock, TX **Attenuation of conflict behavior with cinanserin, a serotonin antagonist: reversal of the effect with 5-hydroxytryptophan and alpha-methyltryptamine.** Research Communications in Chemical Pathology and Pharmacology. 7(1):165-174, 1974.

The brain serotonergic system in behavioral suppression was studied in rats by using cinanserin (2'-(3-dimethylaminopropylthio) cinnamanilide hydrochloride), a serotonin antagonist. The

effect on lever pressing suppression by laboratory rats was reversed by 5HTP. Six albino rats were tested in an experimental chamber. The effects obtained with cinaserin are like those previously described for barbiturates, librium, valium, meprobamate and serax. These findings provide additional support to the speculation that anxiolytics may derive their therapeutic efficacy through alterations in the brain serotonergic system. Results with saline or other solutions is also reported by use of graphs. 19 references. (Journal abstract modified)

176877 Costall, B.; Naylor, R. J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, Yorkshire, England **Possible involvement of a noradrenergic area of the amygdala with stereotyped behaviour.** Life Sciences (Oxford). 11(24):1135-1146, 1972.

The role of a noradrenergic area of the amygdala, the nucleus amygdaloideus lateralis, in the mediation of the sterotypic effects of apomorphine and ET495 was investigated by using the brain lesion technique. It was found that: (1) the nucleus amydaloideus lateralis is involved, either directly or indirectly, with the mediation of the gnawing and biting components of apomorphine and ET485 stereotyped behavior and, therefore, a noradrenergic area may be involved in mediation of a behavior currently considered almost exclusively in terms of dopaminergic events; (2) the integrity of the nucleus amygdaloideus lateralis is not essential for development of the other components of sterotyped behavior, such as sniffing and front limb movements; these repetitive behaviors may be mediated via other brain regions. 15 references. (Author abstract).

176879 Hackman, R.; Pentikainen, P.; Neuvonen, P. J.; Vapaatalo, H. Research Laboratories of Medica Ltd., P. O. Box 325, SF-00101 Helsinki 10, Finland **Inhibition of the apomorphine gnawing compulsion by amantadine.** Experientia (Basel). 29(12):1524-1525, 1973.

The inhibition of the apomorphine gnawing compulsion in rats by amantadine was examined and the effects of the drug were compared to those of some drugs known to act on dopaminergic receptors. Apomorphine was given after treatment with various doses of chlorpromazine, metoclopramide or amantadine or simultaneously with L-dopa. Apomorphine caused dose dependent gnawing compulsion; L-dopa did not induce gnawing but potentiated the effect of apomorphine. Chlorpromazine, metoclopramine and amantadine inhibited dose dependently the gnawing. It is proposed that amantadine has the ability to partially occupy the dopaminergic receptors without causing a marked agonistic action of its own and thus competes with apomorphine at the receptor sites. 7 references. (Author abstract modified).

176963 Lepore, Franco; Ptito, Maurice; Freibergs, Vaira; Guillemot, Jean-Paul. Departement de Psychologie, Universite de Montreal, C.P. 6128, Montreal 101, Quebec, Canada **Effects of low doses of chlorpromazine on a conditioned emotional response in the rat.** Psychological Reports. 34(1):231-237, 1974.

The anxiety reducing effect of chlorpromazine was investigated with 20 rats, divided into two groups. The drugged group received a daily i.p. injection of chlorpromazine, while controls received isotonic saline injections. The heartrate was taken as the index of anxiety. In phase one, both groups were habituated to the testing box and were then given 10 spaced shocks in the testing chamber (conditioned emotional response training). The extinction of the conditioned emotional response was next measured. Results indicate that in all phases the anxiety level was significantly lower for the chlorpromazine group. In the third phase, heartrate recordings were correlated with a specific motor activity. Although heartrate was higher for both groups during activity, the distinction between drugged and normal Ss was maintained. 16 references. (Author abstract)

177019 Sakata, Toshiie; Fuchimoto, Hideaki. First Department of Internal Medicine, Faculty of Medicine, Kyushu University, Fukuoka, Japan **Stereotyped and aggressive behavior induced by sustained high dose of theophylline in rats.** Japanese Journal of Pharmacology (Kyoto). 23(6):781-785, 1973.

Repeated administrations of high doses of theophylline to rats resulting in a series of stages which progressed as treatments were continued, including hypoactivity, stereotypy, killing attack, and automutilation, are discussed. Stereotyped behavior was continuous sniffing with backward locomotion, biting of the cage floor, standing on hind legs with forelimbs flapping, and turning somersaults in the cage. The aggressive behavior associated with theophylline treatment was that seen in affective aggression. The theophyllized killers vigorously attacked animate as well as in-

animate objects including rat pups but never consumed their prey. Possible mechanisms of the effect of theophylline on aggressive behavior are discussed. 13 references. (Journal abstract)

177020 Sakata, Toshiie; Fuchimoto, Hideaki. First Department of Internal Medicine, Faculty of Medicine, Kyushu University, Fukuoka, Japan **Further aspects of aggressive behavior induced by sustained high dose of theophylline in rats.** Japanese Journal of Pharmacology (Kyoto). 23(6):787-792, 1973.

Sustained injection with a high dose of theophylline increased agressiveness in rats in both behavioral ratings and paired fighting. In the latter test, 50% of theophyllized pairs took the fighting position following a hand clap and 75% of the treated rats were dominant over control partners. In the open field test, the theophyllized rat discharged fewer boluses, but there was no change in ambulatory activity. The present results support a previous finding that demonstrated the production of affective aggression with the chronic treatment of theophylline. 7 references. (Journal abstract)

177408 Thompson, Donald M. Department of Pharmacology, Georgetown University Schools of Medicine and Dentistry, Washington, DC 20007 **Repeated acquisition of behavioral chains under chronic drug conditions.** Journal of Pharmacology and Experimental Therapeutics. 188(3):700-713, 1974.

The technique of repeated acquisition of behavioral chains was used to study the chronic effects of phenobarbital, chlordiazepoxide, chlorpromazine, d-amphetamine and methylphenidate. Pigeons worked for food reinforcement in a chamber containing three response keys, all of which were illuminated at the same time by one of four colors. For each session, the task was to learn a new four response chain by pecking the correct key in the presence of each color. Errors produced brief timeout periods, during which the key lights were off and responses had no effect. For comparison, the chronic drug tests were also conducted under a performance condition, in which the behavioral chain was the same from session to session. With the initial error increasing effect of each drug as the reference point, the learning errors during repeated drug administration showed several different patterns, depending on the dose. The behavior was more readily disrupted by the drugs under the learning condition than under the performance condition. Tolerance was more likely to develop to the drug induced increases in errors and pausing (which reduced the rate of reinforcement) than to the drug induced increases in timeout responses (which had no effect on the rate of reinforcement). 12 references. (Author abstract)

177409 Glick, Stanley D.; Jerussi, Thomas P. Department of Pharmacology, Mount Sinai School of Medicine, Fifth Ave. and 100th St., New York, NY 10029 **Spatial and paw preferences in rats: their relationship to rate-dependent effects of d-amphetamine.** Journal of Pharmacology and Experimental Therapeutics. 188(3):714-725, 1974.

Rats were trained to bar press on either a fixed-interval 15 second (FI 15) or fixed ratio (FR 30) schedule for water reinforcement to test spatial and paw preferences under d-amphetamine. Ss were allowed to bar press on either of two left or right levers and most showed consistent side preferences. Rats on the FR 30 schedule were much more sensitive to a drug induced rate decrement than rats on the FI 15 schedule. As rates decreased with increasing drug dose, side preferences reliably increased or decreased depending on the particular pattern of paw use and the relationship between paw and side preferences. In both schedules, baseline rates were directly related to the strength of side preferences. FR 30 Ss with high baseline rates usually used both paws in rapid, alternating, well coordinated movements to bar press; this was disrupted by d-amphetamine such that paws were used individually while bar pressing was at the lower rates. FR 15 Ss used only one paw to make most responses; this was unaffected by the drug. Subtle motor actions of d-amphetamine, possibly a function of altered dopamine metabolism in the nigro-striatal system, may be somewhat responsible for the drug effects on different schedule dependent rates of responding, as well as on spatial and paw preferences. 8 references. (Author abstract)

177410 Leander, J. David; McMillan, D. E. Department of Pharmacology, School of Medicine, Swing Building, University of North Carolina, Chapel Hill, NC 27514 **Rate-dependent effects of drugs. I. Comparisons of d-amphetamine, pentobarbital, and chlorpromazine on multiple and mixed schedules.** Journal of Pharmacology and Experimental Therapeutics 188(3):726-739, 1974.

The effects of d-amphetamine, pentobarbital and chloropromazine on the rate of conditioned key pecking of pigeons under multiple and mixed fixed-ratio 30 fixed-interval 10 min schedules of food presentation were studied. Pentobarbital produced comparable decreases in fixed-ratio response rates under the mixed and multiple schedules; responding under the fixed-interval component of the multiple schedule was suppressed at lower doses than that under the mixed-ratio component. D-amphetamine decreased mixed fixed-ratio response rates more than multiple fixed-ratio response rates, while multiple and mixed fixed-intervals response rates were increased by low doses but decreased by higher ones. Chlorpromazine markedly decreased responding under mixed fixed-ratio components, while only slightly decreasing responding under multiple fixed-ratio components. Responding in fixed-interval components was equally suppressed by chlorpromazine under both schedules. All three drugs exhibited rate dependent effects within the fixed-interval components, increasing the low rates of responding early in the fixed-interval and decreasing the higher rates in the terminal portions of the fixed-interval under both schedules. The control rate below which low rates were increased in the fixed-interval decreased as a function of dose for all three drugs but differed across drugs. 33 references. (Author abstract)

177477 Huston, Joseph P.; Borbely, Alexander A. Institute of Pharmacology, University of Zurich, Gloriastrasse 32, Zurich, Switzerland **The thalamic rat: general behavior, operant learning with rewarding hypothalamic stimulation, and effects of amphetamine.** Physiology & Behavior. 12(3):433-448, 1974.

General behavior, operant learning with rewarding hypothalamic stimulation, and effects of amphetamine were investigated in 52 rats whose major forebrain areas, including the cortex, hippocampus, striatum, amygdala, and septum were bilaterally ablated, resulting in a chronic thalamic preparation. Experiment one measured body temperature and motor activity, showing continuous cyclic 10-60 min rest - activity cycles. Intragastric feeding was followed by periods of quiescence accompanied by hypothermia lasting from 1-5 hrs. Experiment two demonstrated a successful operant conditioning of limb movements in 12 Ss by use of rewarding hypothalamic stimulation. Once a response was strengthened by conditioning, no extinction could be observed, although the response was modifiable by further conditioning. In experiment three, the effects of d-amphetamine included hyperthermia, hyperactivity, and stereotyped behaviors, and the drug facilitated primarily the performance of the previously conditioned behavior. 54 references. (Author abstract)

177533 Mead, Philip G. Keuka College, Keuka Park, NY **Effects of overtraining and pretrial administration of dextroamphetamine on reversal learning in rats.** Perceptual and Motor Skills. 38(2):566, 1974.

The effects of overtraining and pretrial administration of dextroamphetamine on reversal learning in rats were studied. Results of analysis of variance on trials to criterion indicate a significant difference between the overtrained and nonovertrained groups. This lends support to the generality of the overtraining reversal effect. It is contended that the heightened task complexity, together with the small subject pool, provides one explanation for the lack of facilitation found by others under similar conditions. 2 references. (Author abstract modified)

177719 Hoffmeister, F.; Wuttke, W. Institute of Pharmacology, Bayer AG, D-5600 Wuppertal 1, Germany **Negative reinforcing properties of morphine-antagonists in naive rhesus monkeys.** Psychopharmacologia (Berlin). 33(3):247-258, 1973.

Rhesus monkeys were trained to press a lever to extinguish a light associated with a drug infusion scheduled to occur 30 seconds after the onset of the light. Each response during the light period terminated the light for a 1 minute period (avoidance), and a response during the infusion terminated the infusion (escape). The monkeys tolerated a high number of saline infusions. Saline was replaced by nalorphine, cyclazocine, naloxone, cocaine, codeine, pentazocine or propiramfumarate. Infusions of nalorphine and cyclazocine generated avoidance/escape behavior, while infusions of naloxone, cocaine, codeine, pentazocine and propiramfumerate were tolerated. Results show that the morphine antagonists nalorphine and cyclazocine but not naloxone have negative reinforcing properties. 9 references. (Author abstract)

177721 Zebrowska-Lupina, I.; Kleinrok, Z. Department of Pharmacology, School of Medicine, Jaczewskiego 8, 20-090 Lublin, Poland **Behavioural effects of yohimbine administered intraventricu-**

larly in the rat. Psychopharmacologia (Berlin). 33(3):267-275, 1973.

The influence of yohimbine injected into the lateral cerebral ventricle on the behavior of white Wistar rats was investigated. Yohimbine in low doses produced excitatory effects but in high doses it induced central depression. The effect of yohimbine on the action of noradrenaline, amphetamine, hexobarbital, chloral hydrate and ethanol was also examined. 16 references. (Author abstract modified)

177722 Figler, Michael H. Department of Psychology, Towson State College, Baltimore, MD **The effects of chlordiazepoxide (Librium) on the intensity and habituation of agonistic behavior in male siamese fighting fish.** Psychopharmacologia (Berlin). 33(3):277-292, 1973.

The effects of chlordiazepoxide (Librium) on the intensity and habituation of the threat display in male Siamese fighting fish is evaluated by exposing each subject to a male conspecific eliciting stimulus. In an independent groups design, the subjects were tested in either plain tap water or a drug solution. Chlordiazepoxide attenuated threat behavior and facilitated habituation of the display without inducing noticeable sedation. The results were evaluated in terms of a dual process theory of habituation involving independent hypothetical processes of sensitization and habituation which produce the net observed habituation. 45 references. (Author abstract)

177785 Derkach, Peter; Larochelle, Louis; Bieger, Detlef; Hornykiewicz, Oleh. Dept. of Pharmacology, University of Toronto, Toronto, Ontario M5T 1R8, Canada **L-DOPA-chlorpromazine antagonism on running activity in mice.** Canadian Journal of Physiology and Pharmacology (Ottawa). 52(1):114-118, 1974.

The nature of the antagonistic effect of chlorpromazine on L-DOPA induced running activity in mice is studied. Dose - effect relations for L-DOPA, given alone and in combination with chlorpromazine, are determined in male albino mice pretreated with an inhibitor of the extracerebral aromatic L-DOPA dose - response curve. Results are compatible with a noncompetitive blockage of central dopamine receptors by chlorpromazine as the main mechanism of the drug's anti-L-DOPA activity. 20 references. (Author abstract)

177836 de Wied, D.; Sarantakis, D.; Weinstein, B. Rudolf Magnus Institute for Pharmacology, Medical Faculty, University of Utrecht, Vondellaan 6, Utrecht, The Netherlands **Behavioural evaluation of peptides related to scotophobin.** Neuropharmacology (Oxford). 12(12):1109-1115, 1973.

A synthetic pentadecapeptide, desacetylscotophobin analogue (DS 1-15), which differs from the natural product in terms of activity and in structure, was tested in rats in several behavioral tests. To determine the active core of DS 1-15, two other peptides corresponding to the residues 8-15 of the parent molecule (ZS 8-15 and HS 8-15) were tested in the same behavioral situations. These three peptides given in a single subcutaneous injection of 5 micrograms delayed extinction of a pole jumping avoidance response in an equipotent manner for approximately 7 days. In a passive avoidance situation, in which latency to enter a dark box was measured after animals had experienced mild shock 24 hr previously, avoidance latency was increased for several days following a single subcutaneous injection of 5 microgram DS 1-15 and HS 8-15, while XS 8-15 was much less active. None of these peptides affected passive avoidance latency in rats which had no previous shock experience in the dark box. Peptides were virtually inactive in a light - dark preference test and in an open-field test. Discrepancies in data with scotophobin and analogues as reported in the literature may result from differences in aversive stimulation to which animals might have been unintentionally exposed. 28 references. (Author abstract)

177837 Olds, M. E.; Ito, M. Division of Biology, California Institute of Technology, Pasadena, CA 91109 **Effects of chlorpromazine, chlordiazepoxide and pentobarbital on neuronal excitability in the medial forebrain bundle during self-stimulation behavior.** Neuropharmacology (Oxford). 12(12):1117-1133, 1973.

The effects of chlordiazepoxide, chlorpromazine and pentobarbital were studied on self-stimulation behavior and simultaneously on neuronal responses driven by the rewarding stimuli. Rats implanted with microelectrodes in the medial forebrain bundle for recording extracellular potentials and with macroelectrodes in the posterior lateral hypothalamus for producing self-stimulation behavior were tested. The neuronal responses were: (1) an excitatory response in the anterior hypothalamus; and (2) an inhibitory response in the middle hypothalamus. Chloridazepoxide

(20mg/kg), chlorpromazine (4mg/kg) or pentobarbital (10mg/kg) were given intraperitoneally to suppress self-stimulation. Plus-Amphetamine (2mg/kg) was given 30 min later to restore self-stimulation. Chlordiazepoxide and pentobarbital acted nonspecifically on the excitatory response by reducing the spontaneous rate of firing at the time when self-stimulation was suppressed. Chlorpromazine abolished the driven excitatory responses in the anterior hypothalamus which were correlated in a 100% fashion with self-stimulation behavior. All compounds had insignificant effects on inhibitory responses. Results somewhat support suggestions that the effects of chlorpromazine are indices of effects on neuronal activity mediating positive reinforcement. 32 references. (Author abstract modified)

178502 Revusky, Sam; Gorry, Tom Dept. of Psychology, Memorial University of Newfoundland, St. John's, Newfoundland, Canada **Flavor aversions produced by contingent drug injection: relative effectiveness of apomorphine, emetine, and lithium.** Behaviour Research and Therapy. 11(4):403-409, 1973.

Shortly after rats began drinking saccharin solution, different groups of them were injected with different doses of apomorphine, emetine, or lithium. A control group was not injected at all. Six days later, the rats were given free access to saccharin solution and to water. Aversion to saccharin solution was obtained in all injected groups and tended to become more pronounced as the dose level increased. At similiar dose levels, lithium produced the most pronounced aversions, apomorphine produced the weakest aversions, and emetine was intermediate. A followup study with squirrel monkeys confirmed that lithium produces more pronounced aversions than either emetine or apomorphine. From these results, it seems worthwhile to try lithium in the chemical aversion of alcoholism. 8 references. (Author abstract)

178575 Stoff, David M.; Liebling, David S.; Bridger, Wagner H. NIMH, IR, St. Elizabeths Hospital, WAW Building, Washington, DC 20032 **Mescaline hyperreactivity: hallucinations in rats? (Unpublished paper).** Washington, DC, NIMH, 1974. 1 p.

An animal model for human psychosis was developed by studying the effects of mescaline on aversively motivated behavior in rats. The experiments were designed to determine the shock threshold under mescaline and whether repeated unavoidable electric shocks influenced the behavior of rats given mescaline. Preliminary data analyses performed on the response thresholds for the various response categories (no response, flinch - startle, jump, and vocalization) obtained during shock stimulation were inconclusive among drug groups. However, a more conclusive and dramatic result emerged when data analyses were performed on the incidence of jumps and vocalization responses during the intershock period among drug groups. The data indicates that at the higher dose of mescaline rats exhibited behavior during the nonshocked period (i.e.,jumping and vocalizing), a finding which was previously associated with shock stimulation only. These data lend support to the hypothesis that mescaline interfers with signal-reality relationships leading to hallucination.

178638 Schaefer, Gerald J.; Buchanan, Denton C.; Ray, Oakley S. Psychology Research Laboratories, Veterans Administration Hospital, Nashville, TN 37203 **The effects of early p-chlorophenylalanine administration and postweaning housing conditions on serotonin and behavior in rats.** Life Sciences (Oxford). 12(9):401-411, 1973.

The interactive effects of preweaning p-chlorophenylalanine (PCPA) administration and postweaning rearing conditions on brain serotonin (5-HT) levels, body weight, activity in the open field, and active avoidance performance in rats are reported. Rats were given 100mg/kg of PCPA or saline daily from birth until 18 days of age. At weaning (28 days), half of each group was assigned to either an enriched or isolated environmental condition until approximately 80 days of age. A significant drug by environment interaction was found in analysis of 5-HT whole brain levels, which was not related to open field activity but was related to a shock induced active avoidance task. Conditions which decreased 5-HT levels also increased the number of active avoidance responses. The importance of rearing conditions between early drug manipulation and adult testing is discussed. 22 references. (Author abstract)

178756 Babbini, M.; Torrielli, M. V.; Gaiardi, M.; Bartoletti, M.; De Marchi, F. Institute of Pharmacology, University of Bologna, Bologna, Italy **Influence of N1-2-hydroxyethyl substitution on central activity of oxazepam and lorazepam.** Pharmacology. 10(6):345-353, 1973.

The central activities of two N1-2-hydroxyethyl substituted derivatives of oxazepam and lorazepam (SAS 602 and SAS 632), respectively, were compared with those of the parent compounds. It was found that in rats all the drugs had antimetrazol activity and produced muscle relaxant effects and depressive actions upon exploratory behavior. They were all active in facilitating behavior suppressed by punishment, and caused a synchronization of the EEG pattern lasting 4 to 5 h. Both N1-2-hydroxyethyl substituted compounds showed a reduced potency when compared with oxazepam and lorazepam. Compound SAS 632, however, was more active than oxazepam in conflict behavior, with less muscle relaxant activity. This could suggest a usefulness of the compound in clinical applications. 18 references. (Author abstract)

178757 Gumulka, Witold; Kostowski, Wojciech; Czlonkowski, Andrzej. Dept. Exp. Pharmacology, Medical Academy of Warsaw, Warsaw, Poland **Role of 5-HT in the action of some drugs affecting extrapyramidal system.** Pharmacology. 10(6):363-372, 1973.

The effects of drugs influencing the function of the extrapyramidal system, chlorpromazine (CPZ), haloperidol, amphetamine, and oxotremorine, were checked in rats with lesioned MR or DR raphe areas and in animals pretreated with either p-CPA (p-chlorophenylalanine) or LSD, i.e.,during impaired function of the central serotoninergic system. Lesions of the raphe system and pretreatment with either p-CPA or LSD significantly diminished the cataleptogenic effects of both CPZ and haloperidol. The amphetamine induced stereotyped behavior was intensified in animals with raphe system lesions, while in rats pretreated with p-CPA or LSD the action of amphetamine was diminished. Rats with raphe system lesions showed no change in the tremorogenic action of oxotremorine. In animals pretreated with either p-CPA or LSD the onset of the oxotremorine tremor was even delayed. It is concluded that an intact and functionally unimpaired serotoninergic system is necessary for the cataleptogenic action of neuroleptics. 38 references. (Author abstract)

178813 Jarbe, T. U. C.; Henriksson, B. G. University of Uppsala, Dept. of Psychology, Slottsgrand 3, S-752 20 Uppsala, Sweden **Open-field behavior and acquisition of discriminative response control in delta9-THC tolerant rats.** Experientia (Basel). 29(10):1251-1253, 1973.

Open-field (O-F) behavior and acquisition of discriminative response control in delta9-tetrahydrocannabinol (THC) were studied. The hypothesis was tested that if some tolerance occurred, then the cueing effects of TCH should be weakened and discriminative control should therefore develop more slowly in tolerant animals as compared to nontolerant. O-F behavior before and after the presumed development of tolerance was also studied. Subjects were 18 male albino Sprague-Dawley rats. They were randomly divided into three groups of six each. Group 1 was given an ip injection of THC suspended in saline, plus Tween-80 and propylene glycol 30 minutes before the first O-F test. Group 2 received the vehicle before the same test. Group 3 was the control group. All three groups were subjected to discriminative training in a water maze. Findings indicate that all behavioral categories, except urination, differentiated groups 1 and 2 in the O-F test. 9 references.

178867 Boelkins, Richard Charles, II. Stanford University, Stanford, CA **Mother-infant separation: behavioral analysis of an animal model of depression. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. Mfilms, No. 73-4471 HC$10.00 MF$4.00 72 p.

Mother-infant separation in macaque monkeys was investigated to determine if depression occurs and if it could be treated with an antidepressant drug. Six stumptail infants (mean ages 632 days old) and seven irus infants (mean age 584 days old) were each twice separated from their mothers and social groups for 7 day periods. The Ss were administered Elavil or saline control during the first or second separation. The grooming of the Ss by mothers and peers significantly increased during the reunion periods. There were significant decreases in the frequency of social play with peers and exploration of the physical environment. The antidepressant drug significantly reduced the depressive posture of huddling, which occurred more often in stumptail and in the younger Ss. No further significant effects due to drug treatment were detectable. It is concluded that the experimental paradigm, separation by removal of infant, rather than removal of mother, is unlikely to produce depression; that antidepressant drug treatment is not notably therapeutic; and animals as old as 3 years respond to reunion with mother in virtually the same way as do infants only 4 or 5 months old. (Journal abstract modified)

179990 Barrett, Robert J.; Steranka, Larry R. Psychology Research Laboratory, Veterans Administration Hospital, Nashville, TN 37203 **An analysis of d-amphetamine produced facilitation of avoidance acquisition in rats and performance changes subsequent to drug termination.** Life Sciences (Oxford). 14(1):163-180, 1974.

An analysis of d-amphetamine produced facilitation of avoidance acquisition and performance changes subsequent to drug termination is presented. In Experiment 1 rats were trained on a discriminated Y-maze active avoidance task following administration of saline or one of three dosages of d-amphetamine. The six measures recorded simultaneously during each session indicated that the avoidance facilitation produced by d-amphetamine was due to attenuation of shock induced behavioral suppression resulting in a behavioral baseline more compatible with the animal's associating running with shock avoidance. Results showed that the avoidance decrement following drug termination is dependent on training dosage and whether the drug is abruptly or gradually withdrawn. This experiment suggested that the disruption is due to dissociation between the drug and nondrug states and could be attenuated by gradually withdrawing the drug over training sessions. 19 references. (Author abstract)

180021 Gianutsos, Gerald; Drawbaugh, Richard B.; Hynes, Martin D.; Lal, Harbans. Dept. of Pharmacology and Toxicology, College of Pharmacy, Univ. of Rhode Island, Kingston, RI 02881 **Behavioral evidence for dopaminergic supersensitivity after chronic haloperidol.** Life Sciences (Oxford). 14(5):887-898, 1974.

The overt symptoms of animals treated with and then withdrawn from haloperidol were studied. Chronic administration for 16 days of haloperidol (in increasing doses) resulted in a supersensitivity of dopamine receptors. This supersensitivity was manifested by an enhanced stereotypy and aggression in response to small otherwise ineffective doses of apomorphine. Maximum aggression was observed 7 days after the last dose of haloperidol when 2.5mg/kg of apomorphine was administered. In addition, wet shakes, reminiscent of withdrawal from morphine, are observed in these animals after cessation of the haloperidol administration. These shakes were blocked by morphine. These results may be interpreted to mean that wet shakes and drug induced aggression are the results of hyperactivity of the dopaminergic system. 28 references. (Author abstract modified)

180044 Johansson, G. Institute of Physiology, University of Helsinki, Finland **Inhibitory effect of doxepin on agonistic behaviour elicited by hypothalamic stimulation in the cat.** In: Psychiatria Fennica. Helsinki, Helsinki University Central Hospital, 1973. 301 p. (p. 241-248).

The effect of the tricyclic antidepressant doxepin on the agonistic behavior provoked in the cat by electrical stimulation of the hypothalamus was studied using bipolar steel wire electrodes. Responses of mydriasis, piloerection, behavioral alerting, hissing, attack, and motor activity were rated after various quantities of doxepin. The lowest dose had no effect, 5mg/kg depressed behavioral alerting and motoractivity, and 10mg/kg depressed all responses except mydriasis which was depressed after 15mg/kg. 25 references.

180061 Kjellberg, B.; Randrup, A. AB Ferrosan, Pharmacological Department, Malmo, Sweden **Stereotypy with selective stimulation of certain items of behaviour observed in amphetamine-treated monkeys (Cercopithecus).** Pharmakopsychiatrie Neuropsychopharmakologie (Stuttgart). 5(1):1-12, 1972.

The behavioral effects of a single dose of d-amphetamine were studied in experiments on primate monkeys (Cercopithecus aethipos and sp.). Amphetamine produces selective stimulation of certain behavioral items and decrease of others resulting in a behavior with stereotyped character. In contrast with rats abnormal behavior was also seen 24 to 176 hours after the injection of amphetamine. Certain items of behavior are still selectively stimulated but are now not done continuously, grooming and other items of normal behavior are interspersed. Temporary reappearance of more stereotyped behavior is observed. The selective stimulation with stereotypy seem to be an effect of amphetamine which is common to all mammals including man. 22 references. (Author abstract)

180591 Kerpel-Fronius; Sandorne. Psychological Institute, Hungarian Academy of Sciences, Budapest, Hungary **/Reflection of short-term light adaptation effect in the electroretinogram./** Rovid tartamu fenyadaptacio hatasanak tukrozodese az elektroretinogramban. In: Kornyezet es Tevekenyseg. Budapest, Akademiai Kiado, 1972. 681 p. (p. 39-42).

Effects of short-term light adaptation as reflected in a retinogram were studied. The effect of blue and red colors on the electroretinogram of cats in chlorasole narcosis (i.p. 60mg/kg) with urethane (250mg/kg) was investigated. Variation of the period of the first stimulus (blue), did not produce significant variation of the response. Red light as the first stimulus resulted in great variations. Response to the second stimulus declined to 1200 msec. Deviations were statistically significant in the case of blue light, while significant deviations for red light were found at 1200 msec only. Response to the variation of the interval between stimuli did not differ with respect to color. Significance values did not permit unambiguous conclusions. The response to the blue stimulus can be explained on a purely photochemical basis, while with red light the activity of neural factors must also be assumed.

180724 Baruk, Henri. 5, quai de la Republique, 94-St. Maurice, Paris, France /**Experimental catatonia and psychopharmacology.**/ Catatonie experimentale et psychopharmacologie. Therapie (Paris). 27(1):119-131, 1972.

Pharmacologically induced catatonia in animals is examined as a good indicator of psychotropic activity in man. Six major symptoms of Kalhbaum's Catatonia; attitude in bending, catalepsy, active or passive depression, hyperactivity, organovegitative problems, and loss of the will to live are outlined. A history of experimental catatonia in animals, from its discovery by de Jong and H. Baruk in 1928 to current research in biochemical factors, is presented. The term, 'Poisons of the will,' as originated by Baruk, is applied to symptoms of catatonia. 4 references. (Author abstract modified)

181384 Ueki, Showa; Ogawa, Nobuya; Gomita, Yutaka; Yamamoto, Tsuneyuki; Araki, Yasunori; Ogasawara, Takashi; Hara, Chiaki; Fujiwara, Ryoichi. Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka, Japan **Behavioral pharmacology of bromazepam (Ro 5-3350), a new benzodiazepine derivative.** Igaku Kenkyu (Fukuoka). 43(1):41-58, 1973.

Behavioral effects of bromazepam, a new derivative of benzodiazepine, were investigated in mice and rats and compared with those of diazepam and chlorpromazine. The results indicate that bromazepam has pharmacological properties qualitatively similar to those of diazepam and is of greater potency as a minor tranquilizer. The effects of bromazepam are particularly potent in suppressing aggressive behavior and conditioned avoidance responses. It is expected that bromazepam has some characteristic effects different from those of diazepam in its clinical uses. 22 references. (Journal abstract modified).

181386 Nishizaki, Hiroyuki; Hiraiwa, Toru; Ito, Ryuta; Takai, Akira. Toho University, Tokyo, Japan **Comparison of clopenthixol and perphenazine in behavior and EEG of unanesthetized cats.** Journal of the Medical Society of Toho University (Tokyo). 18(1):95-114, 1971.

A thioxanthene derivative, clopenthixol (Sord), was compared to perphenazine (PZC) in behavior and EEG modification in an unanesthetized cat with a chronic implanted electrode. The site of action was explored by the changes in electrically induced behaviors belonging to the sympathetic and parasympathetic nerve center. Low doses of Sord induced immediate rest, sleep, and the prolongation and frequent appearance of REM sleep. High doses induced excitation and ataxia. Under both nonstimulation and stimulation, it acted on the hypothalamus and the parasympathetic nerve center. The action of PZC was similar to that of Sord except for the superiority of the tranquilizing effect in PZC and of REM sleep and the hypnotic effect in Sord. These results suggest a clinical application for the induction of REM sleep with Sord in addition to its use as a tranquilizer. 17 references. (Journal abstract modified).

181396 Killam, Keith F. University of California, Davis, CA **Drugs on EEG correlates of behavior.** Psychopharmacology Bulletin. 10(1):66, 1974.

The brain response to visual and auditory conditioned stimuli and the modification of these responses by tranquilizers, stimulants and depressants are described. Findings from electroencephalographic (EEG) studies of cats show reliable changes in EEG patterns during conditioning which were altered by atropine sulfate, lysergic acid diethylamide (LSD), chlorpromazine and trifluoperazine. The administration of acute, low doses of diazepam produced spindle like bursts in monkeys' and baboons' EEG patterns from the frontal and parietal cortex. Higher doses caused a slowing of the alpha rhythm and an increase in the low frequency electrical activity of the cortex and hippocampus. Similar change occurred initially during chronic administration; however, after five to six days of chronic use, alpha rhythm

was faster than normal, and it returned to normal 10 days after the drug was discontinued. Other studies with cats revealed that physostigmine increased the number of errors and delayed performance in a discrimination task.

181397 Mitchell, Clifford L. University of Iowa School of Medicine, Iowa City, IA **Neuropharmacology of psychopharmacological agents.** Psychopharmacology Bulletin. 10(1):66-67, 1974.

The effects of various psychopharmacological agents on pain resulting from tooth pulp and radial nerves stimulation are described. Results of studies in animals in which electrical shocks were delivered to the tooth pulp revealed chlorpromazine to be half as effective as morphine in altering the threshold voltage required to elicit a jaw jerk in cats. Individual variations were much greater among dogs than among cats. Effects of phenobarbital on electroencephalographs during classical aversive training of cats are reported.

181399 Dews, Peter. Harvard University, Boston, MA **Basic types of effects of drugs on behavior.** Psychopharmacology Bulletin. 10(1):67-68, 1974.

The effects of drugs used singly or in combination on reproducible patterns of behaviors in animals is described. Chlorpromazine, a barbiturate, morphine and amphetamine were administered to animals trained to behave in predictable patterns. Monkeys showed the effects of chlorpromazine and amphetamine were not influenced by the type of motivation. Chlorpromazine decreased pigeons' pecking but did not affect their ability to discriminate between green and blue lights. Reserpine reduced responding in pigeons; but amphetamine, pipradrol or cocaine, given after reserpine, improved the pecking responses. Amphetamine treated pigeons surpassed methyltryptamine treated pigeons in increased pecking responses. Drug effects were more dependent on the established response rate of the behavior than on the causes and other attributes of behavior. Related studies indicated that a tryptaminergic mechanism is responsible for behavioral inhibition.

181400 Gollub, Lewis R. University of Maryland, College Park, MD **Experimental studies in comparative psychopharmacology.** Psychopharmacology Bulletin. 10(1):68-69, 1974.

Studies in pigeons and rats designed to elucidate the interaction between psychopharmaceutical agents and behavioral test baselines are described. Behavioral responses are conditioned under various schedules of operant reinforcement, and continued training is given until responding becomes stable. Drugs are administered parenterally before experimental sessions. Findings indicate that intermediate dose levels of pentobarbital, phenobarbital and alpha chloralose increased overall response rate and systematically changed the temporal pattern of responses in pigeons. Similar results were obtained in rats exposed sequentially to two different values of fixed-interval schedules under d-amphetamine treatment. Related studies using d-amphetamine and chlorpromazine call into question the practice of administering drug amounts of these compounds proportional to body weights.

181401 Jarvik, Murray E. Yeshiva University, New York, NY **Behavioral effects of drugs in Macaca mulatta.** Psychopharmacology Bulletin. 10(1):69-70, 1974.

The effects of drugs on short-term memory and discrimination learning in monkeys are described. Scopolamine was found to markedly impair accuracy in delayed response tests, while chlorpromazine greatly decreased the rate of response but did not affect accuracy. The retention phase of memory was less susceptible to the effects of scopolamine than either the registration or retrieval phase of the process; but under certain circumstances, a definite effect on retention was demonstrated. Short-term retention was impaired by tetrahydrocannabinol extract and marihuana cigarettes. Related studies suggest that smoke without nicotine is repugnant, and drugs which block nicotine may inhibit smoking by humans.

181402 Kornetsky, Conan. Boston University, Boston, MA **Neuropsychopharmacological studies of attention.** Psychopharmacology Bulletin. 10(1):70, 1974.

Effects of psychopharmacological drugs on attentive processes are reported. When electrical stimulation to the reticular formation was given along with chlorpromazine (CPZ), performance that was impaired by either alone was not different from that seen after saline alone. This effect may be similar to the calming action of CPZ in the overaroused state of chronic schizophrenics. Low levels of stimulation to the rat reticular formation improved performance on

some tasks. Behaviors which are characterized by high response rates were significantly more vulnerable to the depressive effects of imipramine than to desipramine, suggesting that imipramine may be the preferred therapeutic agent in cases of depression accompanied by motor agitation.

181403 Laties, Victor G. University of Rochester, Rochester, NY **Effects of psychopharmacologic agents on behavior.** Psychopharmacology Bulletin. 10(1):70-71, 1974.

Drug effects and neurochemical processes were studied in an attempt to correlate them with behavior. Fine details of behavior responses are examined in a variety of species. For most experiments, animal subjects are trained to work for food reward in studies controlled by on-line computers. Results indicate that changes in the behavior situation can be used to offset drug effects. The use of computer technology in the investigations is detailed.

181404 McGaugh, James L. University of California, Irvine, CA **Drug effects on learning and memory.** Psychopharmacology Bulletin. 10(1):72, 1974.

The effects of drugs that affect memory on various types of learning are described. Studies in rats and mice indicate that pretrial injections of strychnine facilitate learning, while posttrial injections of strychnine, pitrotoxin, megimide, and metrazol enhance avoidance learning. During discrimination learning, strychnine, metrazol and picrotoxin enhanced performance. Pretrial and posttrial systemic injections of pentylenetetrazol, as well as implantation of strychnine crystals in the mesencephalic reticular formation, enhanced discrimination learning. In studies of the amnesic effects of electroconvulsive shock and drugs, prelearning and postshock injection of strychnine attenuated the degree of amnesia.

181405 McMillan, Donald E. University of North Carolina, Chapel Hill, NC **Determinants of drug effects on punished behavior.** Psychopharmacology Bulletin. 10(1):72-73, 1974.

Why mild tranquilizers and sedatives cause a resurgence of behavior that has been suppressed by punishment was studied. Preliminary findings indicate that chlordiazepoxide increases the rates at which pigeons emit punished responses but decreases the rate of unpunished responses, while chlorpromazine increases neither rates of punished nor unpunished responding. The effects of these drugs on punished behavior seem to depend on the control of the rate of responding, the punishment intensity and the schedule of positive reinforcement. The effects of two marihuana extracts and mescaline were similar to those of major tranquilizers.

181406 Russell, Roger W.; Cotman, Carl W. University of California, Irvine, CA **Mechanisms of drug-induced behavioral tolerance.** Psychopharmacology Bulletin. 10(1):73, 1974.

An attempt to correlate a number of behavioral patterns with neurochemical parameters is described. Preliminary results of biochemical studies on whole brain homogenates of chronically diisopropylfluorophosphate (DFP) treated rats revealed that acetylcholine levels were elevated and remained at 140% of normal; the activity of choline acetyltransferase was unchanged; and the activity of cholinesterase was reduced and remained at 27% of normal. Findings suggest that feedback inhibition of the synthesis of acetylcholine is not associated with the development of behavioral tolerance to DFP. Challenge studies indicated that DFP treated rats were more sensitive to the behavioral effects of quaternary cholinolytic drugs than control rats but were less sensitive to the behavioral effects of cholinomimetic agents. One mechanism that may underlie the development of behavioral tolerance to DFP is a reduction in the sensitivity of cholinergic receptors to acetylcholine.

181408 Leeming, Frank C. Memphis State University, Memphis, TN **Modification of the frustration effect with drugs.** Psychopharmacology Bulletin. 10(1):71, 1974.

The effects of tranquilizers and antidepressants on the magnitude of frustration are reported. The general technique in investigations was to deprive rats of a reinforcing agent in a situation in which it was previously given. Preliminary findings revealed that food or water deprivation do not affect the magnitude of the frustration effect.

181605 Glow, Peter H.; Russell, Alan. University of Adelaide, Adelaide, South Australia 50001 **Sensory-contingent barpressing for familiar and novel change under a dexamphetamine-amylobarbitone mixture.** Animal Learning & Behavior. 2(1):27-30, 1974.

In three experiments the effects of the administration of Drinamyl (a mixture of dexamphetamine and amylobarbitone in the ratio of 1:6.5by weight) on responding for novel and familiar sensory change was examined. In the first experiment, an acute administration of Drinamyl enhanced sensory contingent barpressing (SCBP) with no differential for novel vs. familiar change. In the second experiment, acute Drinamyl also enhanced SCBP, with a larger effect for novel change. In a third experiment, the effect of chronic Drinamyl administration was studied. Responding was substantially increased, with responding for sound change showing a greater effect than for light change. Responding for sound change also increased markedly over trials. When the sensory reinforcers were deleted, responding declined. The results were interpreted in terms of an increase in the reward value of SCBP under the drug. The three phases of response in the rats are also outlined. 11 references. (Journal abstract modified)

181654 Nakajima, Ryoko; Saji, Yoshiaki; Kozato, Yoshiaki; Mikoda, Reiko; Tanayama, Shigeharu; Nagawa, Yuji. Takeda Chemical Industries, Ltd., Osaka, Japan **Dissociative change in anti-aggressive and muscle relaxant actions of s-Triasolobenzodiazepine (D-40TA) by repeated administration and phenobarbital pretreatment, and its relation to metabolism.** Journal of the Takeda Research Laboratories (Osaka). 32(3):264-274, 1973.

Dissociative change in antiaggressive and muscle relaxant reactions of s-triasolobenzodiazepine (D-40TA) by repeated administration and phenobarbital pretreatment and its relation to metabolism were investigated. Nine or 12 day treatment with D-40TA developed tolerance to its skeletal muscle relaxant action, but not to its antiaggressive action, i.e.,antifighting and antimuricidal actions in mice and rats. Similar pharmacological dissociation of D-40TA was also observed by pretreatment of phenobarbital for 3 days. Studies on the brain distributions of D-40TA and its metabolites using 14C-labeled D-40TA in rats suggest that only a rapid decay of muscle relaxant activity of D-40TA after phenobarbital pretreatment is due to metabolic acceleration but that other pharmacological dissociation occurs due to an alteration of neuronal sensitivity to D-40TA and metabolite B in the brain sites which are responsible for muscle relaxant and antiaggressive actions, respectively. 15 references. (Author abstract modified)

182103 Tsuchie, Fumiyo; Nakanishi, Hitoshi; Kaneto, Hiroshi. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Nagasaki University, Nagasaki, Japan **Attempt to evaluate the physical dependence liability of psychotropic drugs in mice.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):92, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the physical dependence liability of psychotropic drugs in mice was evaluated. Mice were rendered physically dependent on morphine or barbiturates. On natural withdrawal from these drugs the following abstinence syndrome was commonly elicited: restlessness, hyperreaction, urination, defecation, sniffing, rearing, peeping below, washing, grooming, wet dog shaking and jumping. In the case of morphine dependent mice, the signs were masked with the narcotics while tranquilizing drugs used here behaved as partial and nonspecific depressants, confirming the agreed facts that the latter group of drugs could not be the essential substituents for the opiate. The withdrawal signs which developed on barbiturate dependent mice were suppressed by meprobamate, chlordiazepoxide and diazepam, the dependence liability of which have been well documented clinically and experimentally, but not by morphine. (Author abstract modified)

182104 Yanaura, Saizo; Tagashira, Eijiro. Hoshi College of Pharmacy, Tokyo, Japan **Drug dependence test of phenobarbital and morphine in rats by spontaneous intake.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):92, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the intake of drug containing feed with taste adjusted placebo feed was compared. An experimental technique was established to investigate whether there were differences in the type of preference formation among various groups of substances. The male and female rats were bred individually in a cage with two feed containers each. The two containers were exchanged in the position daily to avoid space orientation of the animals. The type of preference formation for morphine containing feed showed differences from the preference formation for phenobarbital containing feed. Abstinence symptoms as the sign of physical dependency after giving morphine and phenobarbital were severe and a

relatively long time was required for recovery. Individual differences and sex differences were observed in the preference formation and in the occurrence of abstinence symptoms. (Author abstract modified)

182107 Schintomi, Keiichi; Yamamura, Michio; Kowa, Yoshio. Osaka Research Division, Biological Research Laboratory, Tanabe Seiyaku Co., Ltd., Osaka, Japan **Effects of psychotropic drugs on methamphetamine-induced excitations in the aggregated mice.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):94, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the effects of psychotropic drugs on methamphetamine induced excitations in aggregated mice were reported. The following two excited behaviors were observed: a hyperactivity characterized by constant running around and jumping, and a fighting behavior with violent squeak. The effects of various drugs on both behaviors were investigated and the following results were obtained. Some of the drugs tested, according to the minimal effective doses which inhibited fighting and hyperactivity, respectively, were: haloperidol, clothiapine, perphenazine, thiothixene, chlorpromazine, chlorprothixene, diazepam, phenobarbital-Na, methaqualone, promethazine, ethopromazine, and benzylimidazoline. Major tranquilizers selectively inhibited the methamphetamine induced excitations at very low doses, as compared with fighting in mice by Tedeschi et al. Minor tranquilizers depressed only fighting behavior, and antidepressants or other drugs did not inhibit the excitations. The results indicate that this method may be available for the evaluation of major tranquilizers. (Author abstract modified).

182108 Horibe, Masayuki; Sano, Mitsuaki; Yamamoto, Hiromi; Kobayashi, Masafumi; Sato, Mikio. Department of Pharmacology, Nihon University School of Dentistry, Tokyo, Japan **The effect of methamphetamine on brain ACh consumption and aggressiveness in mice stressed mildly by long term isolation.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):94, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the effect of methamphetamine on the relation between aggressiveness and its brain acetylcholine consumption ratio of isolated and aggregated mice was reported. Aggressive degree in methamphetamine (M) administered and ringer solution (RGR) fed mice was lowered in comparison with that of intact (INT) mice. Behavior in M-mice was more provoked than in RGR mice at the third week of experimental breeding, although the difference of both was not remarkably apparent after this week. The ratio of INT aggressive mice was significantly enhanced in comparison with that of INT nonaggressive mice. The ratio of M aggressive mice was significantly lowered in comparison with that of the INT aggressive mice. (Author abstract modified)

182109 Ushijima, Itsuko; Ono, Nobufumi; Furukawa, Tatsuo. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Fukuoka University, Fukuoka, Japan **Influences of lithium on the behavioral action of methamphetamine and tetrabenazine.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):95, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the behavioral effects of lithium in mice were reported. There were no differences between lithium and saline groups in the increase of body weight and spontaneous activities. Tetrabenazine brought about an increase of locomotor activities in mice treated 24 hours previously with nialamide and this increase in the activities tended to be inhibited by lithium. The enhancement in locomotor activities and stereotyped behavior induced by subcutaneous injection of methamphetamine were seen to be inhibited in lithium treated mice as compared with the saline group. Tetrabenazine induced a slight increase and subsequent decrease of locomotor activities in lithium treated mice while it brought about simply a decrease of the activities in saline treated mice. The similar results were obtained when tetrabenazine was injected in mice treated 2 hours previously with a single administration of lithium. From the results, it is suggested that the actions of methamphetamine and tetrabenazine are modified by lithium. (Author abstract modified)

182110 Ando, Kiyoshi; Yanagita, Tomoji. Medical Research Laboratory, Central Institute for Experimental Animals, Nogawa, Kawasaki, Japan **Effects of CNS stimulants on operant behavior.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):95, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the effects of d-amphetamine, methamphetamine, pipradrol and caffeine on Sidman avoidance and differential

reinforcement of low rate (DRL) schedule for food reinforcement in rats were reported. In Sidman avoidance, all drugs except caffeine showed an increment in response rate. In the DRL schedule, d-amphetamine showed a remarkable interresponse time (IRT) mean decrement, but IRT variance was unchanged. Methamphetamine showed a minimum IRT mean and an increment of IRT mean and variance. In pipradrol, IRT mean and variance increment were observed; although some rats showed an IRT mean decrement and an unchanged variance similar to that of amphetamines. Although, by gross behavior observation, all drugs stimulated spontaneous motor activities, different effects on response rate and IRT mean were observed. The changes in IRT variance and timing discriminability score indicate the different effects of CNS stimulants on the timing process of animal behavior. (Author abstract modified)

182111 Tanabe, Kenzaburo; Maki, Eiji. Research Laboratories, Nippon Merck-Banyu Co., Ltd., Okazaki, Aichi, Japan **Effects of cyproheptadine on the eating behavior of rats and cats.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):96, 1972.

At the 45th meeting of the Japanese Pharmacological Society, it was reported that cyproheptadine, a potent antiserotonin and antihistamine agent, increased food intake in cats. Frequency and amplitude of the spontaneous EEG in the lateral hypothalamic area, the feeding center, were also increased following the same doses of cyproheptadine. These electroencephalogram (EEG) responses disappeared after satiating the animal with a meal. Chlorpromazine reduced the food intake. In anesthetized cats, cyproheptadine showed no significant change in the glucose difference between the femoral artery and vein. Physostigmine induced EEG arousal reaction in unanesthetized cats was markedly shortened after intravenous injection of cyproheptadine. Cyproheptadine and anticholinergic agents such as scopolamine and benztropine produced an increase in number of responses emitted by rats trained to lever press for food reward. Physostigmine markedly reduced the number of responses. The locomotor activity of rats did not increase following cyproheptadine and the anticholinergic agents tested. These results indicate that cyproheptadine enhanced activity of the feeding center, thereby producing the eating behavior. (Author abstract modified)

182112 Tadano, Takeshi; Sakurada, Shinobu; Nishioka, Masaki; Kisara, Kensuke. Department of Pharmacology, Tohoku College of Pharmacy, Sendai, Japan **Effects of LiCl on the central nervous system.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):96, 1972.

At the 45th meeting of the Japanese Pharmacological Society, it was reported that LiCl decreased the spontaneous activity of mice measured by either the wheel cage or the photocell counter method. ID50 for the spontaneous motor activity obtained by the wheel cage method was 700mg/kg. The effect of LiCl on conditioned avoidance responses of mice was examined by the pole climbing method. LiCl at a dose of 600mg/kg inhibited markedly conditioned avoidance responses but not unconditioned ones. LiCl at a dose of 400mg/kg produced hypothermia, which reached a maximum 60-90 min after injection. LiCl in doses of 200mg/kg or more potentiated hypnosis induced by barbiturates. LiCl, even in doses above 600mg/kg, caused neither loss of righting reflex nor catalepsy. LiCl at a dose of 600mg/kg inhibited the biting and attacking in electroshock induced aggressive behavior consisting of attacking, biting, vocalization, immobility and piloerection. (Author abstract modified)

182114 Fujiwara, Michihiro; Ogawa, Nobuya; Ueki, Showa. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Sapporo, Japan **Effects of psychotropic drugs on abnormal behavior induced by delta9-tetrahydrocannabinol.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):98, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the effects of various psychotropic drugs on abnormal behavior induced by delta9-tetrahydrocannabinol (THC) in female rats were reported. Effects on muricide were examined in rats which continued this behavior for more than 5 days after injection of THC at a state of individual housing. THC induced muricide was inhibited by atropine (AT), trihexyphenydyl (THP), promethazine (PMZ), methamphetamine (MAP), imipramine (IMP), chlorpromazine (CPZ), haloperidol (HPD), and diazepam (DZP). Walking back and pivoting were decreased by AT, YHP and DZP, but unaffected by IMP. Catalepsy was inhibited by AT, THP and PMZ at much smaller doses than those which suppressed muricide, and also by MAP and IMP, whereas it was potentiated by CPZ, HPD and DZP instead. THC induced catalepsy was sensitive especially to the effect of

antiparkinsonism drugs such as THP, PMZ and AT. (Author abstract modified)

182115 Gomita, Yutaka; Ogawa, Nobuya; Ueki, Showa. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Sapporo, Japan **Effects of psychotropic drugs on discrimination avoidance conditioning in rats with olfactory bulb ablations.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):98, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the effects of various psychotropic drugs on acquisition of discrimination conditioning in olfactory bulb rats were reported. Methamphetamine caused marked increases in both the CRs to positive and negative CS and thus impaired discrimination. Amitriptyline decreased the CRs to negative CS, without affecting the CRs to positive CS and thus resulted in good discrimination. Chlorpromazine impaired the discrimination, because both the CRs to positive and negative CS were decreased. Chlorpromazine facilitated acquisition of the CRs to positive CS, while it decreased that to negative CS instead, and therefore caused better discrimination than that in a control group. (Author abstract modified)

182116 Tadokoro, Sakutaro; Ogawa, Haruyoshi. Department of Pharmacology, School of Medicine, Gunma University, Maebashi, Japan **Behavioral-pharmacological studies on tricyclic antidepressants in rats.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):99, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the behavioral pharmacological effects of imipramine, amitriptyline and doxepin in rats trained on schedules of FR 30 and FI-1 for food, and continuous and discriminated avoidance were reported. When single doses were administered orally, these drugs mainly showed suppressive effects like chlorpromazine on respondings in all the schedules. Conditioned emotional response (CER) developed by stimulus presentation associated with electric shock under FR and FI schedules was not attenuated. Doxepin showed similar effects of amitriptyline rather than that of imipramine. These effects persisted for more than 10 days after the withdrawal. When 50mg/kg/day were given for 15 days, tolerance was produced against the inhibitory effect. Rates of responding in the avoidance schedules returned to baseline immediately after the withdrawal. It was noted that repeated administrations of tricyclic antidepressants revealed complex effects, mixing selective enhancement or tolerance, depending on dosing and experimental indicators. (Author abstract modified)

182117 Ogawa, Haruyoshi; Tadokoro, Sakutaro. Department of Pharmacology, School of Medicine, Gunma University, Maebashi, Japan **Effects of consecutive administration of diazepam and doxepin on both approach-withdrawal and approach-avoidance responses in rats.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):99, 1972.

At the 45th meeting of the Japanese Pharmacological Society, doxepin was examined for a diazepam like effect. Consecutive administration of diazepam increasingly enhanced its attenuating effect against the suppression of respondings in two different schedules. While repeated administration of doxepin did not exhibit any diazepam like effect for 1 to 2 weeks, after 2 to 3 weeks' administration, clear diazepam like effect was observed in approach - withdrawal schedule. Potency was rather weaker than that of diazepam. In the approach - avoidance conflict schedule only a little effect was exhibited. It is concluded that doxepin revealed diazepam like effects only after long-term administration. (Author abstract modified)

182128 McKenzie, G. M.; Viik, K.; Bover, C. E. Department of Pharmacology, Wellcome Research Labs, Research Triangle Park, Durham, NC 27709 **Selective blockade of apomorphine-induced aggression and gnawing following fenfluramine or raphe-lesions in the rat.** Federation Proceedings. 32(3):248, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of drugs and electrolytic lesions on apomorphine induced fighting and stereotyped behavior studied in Long Evans, male rats were reported. Bilateral electrolytic lesions in a variety of dopamine rich nuclei failed to block either the apomorphine induced fighting or gnawing. Lesions in the paraventricular gray matter, at the level of the dorsal raphe nucleus, prevented the induction of aggression with apomorphine. In addition, lesioned animals failed to perform the characteristic gnawing behavior following large doses of apomorphine but, instead, responded with stereotyped sniffing and licking characteristic of low doses of apomorphine. Haloperidol blocked the apomorphine induced aggression, stereotyped

gnawing and stereotyped sniffing and licking. In contrast to haloperidol, fenfluramine blocked the aggressive response and the stereotyped gnawing but did not block the stereotyped sniffing and licking. These results suggest that central lesions or drugs suspected of influencing central serotonergic mechanisms block apomorphine induced aggression and stereotyped gnawing but not stereotyped sniffing and licking. An alternate interpretation, in the case of fenfluramine, may be that this agent selectively blocks dopamine receptors involved in the fighting and gnawing responses but not those receptors responsible for stereotyped sniffing and licking. (Author abstract)

182131 Van Tyle, W. Kent; Burkman, A. M. Division of Pharmacology, College of Pharmacy, Ohio State University, Columbus, OH 43210 **Disposition of norapomorphine and N-n-propylnorapomorphine in mouse brain and its correlation with stereotyped gnawing behavior.** Federation Proceedings. 32(3):248, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the disposition of norapomorphine (NAP) and N-n-propylnorapomorphine (PNAP) in mouse brain and its correlation with stereotyped gnawing behavior were reported. Following intravenous administration, the peak brain concentration of PNAP was reached within 1 minute, and at this time 4.7% of the administered dose was found in brain. In contrast, the peak brain concentration of NAP occurred 5-10 minutes following intravenous administration at which time 0.9% of the dose was found in brain. A positive correlation between the incidence of stereotypical gnawing behavior in mice and the brain concentration of apomorphine for both NAP and PNAP and was found to be 21.05nM/gm and 3.05nM/gm, respectively. (Author abstract modified)

182133 Dragovich, James A.; Margules, D. L.; Margules, Adrienne S. Temple University, Philadelphia, PA **Determinants of the noradrenergic satiety effect: environmental darkness vs. the feeding pattern.** Federation Proceedings. 32(3):275, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, a study of the determinants of the noradrenergic satiety effect in relation to environmental darkness vs. the feeding pattern were reported. Chow intake was restricted to the light portion of the daily cycle (1900-0700 EST). Five male albino rats, implanted with bilateral cannulas aimed for the lateral hypothalamus, were adapted to this schedule for 2 weeks. Water was available ad lib. They were treated with l-norepinephrine (l-NE) administered bilaterally, immediately prior to a 1 hr. milk feeding test, which occurred at different times in the light at weekly intervals. None of the points in the light showed a significant drug induced change except the 2000 hr. point, which showed a suppression. This is the time nearest to the termination of darkness and the time of maximal deprivation. Apparently forcing rats to eat only in the light is not sufficient to cause l-NE to suppress milk intake. In contrast, all treatments with l-NE in the dark produced significant suppressions of milk intake. Thus, l-NE suppresses milk intake in the dark regardless of whether the rats are fed ad lib or food deprived. The environmental cycle of light and darkness is more influential than the feeding pattern in determining the effects of intrahypothalamic l-NE. (Author abstract modified)

182136 Ervin, G. N.; Smith, G. P. E. W. Bourne Behavior Research Lab, Department of Psychiatry, New York Hospital, Cornell Medical Center, White Plains, NY 10605 **Decreased anorexia, excitement and stereotypy to d-amphetamine after lateral hypothalamic 6-hydroxydopamine (6-OHDA) injections.** Federation Proceedings. 32(3):276, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, decreased anorexia, excitement and stereotypy to d-amphetamine after lateral hypothalamic 6-hydroxydopamine (6-0HDA) was reported. 6-OHDA was microinjected bilaterally into the anterior hypothalamus at the caudal edge of the optic chiasm at lateral or medial sites. Such injections decrease hypothalamic and forebrain, norepinephrine, but do not change striatal dopamine. Anterolateral 6-OHDA decreased the anorexia, excitement and stereotypy produced by d-amphetamine in 5 of 9 rats and decreased the anorexia only in 3 of the same 9 rats. Anteromedial 6-OHDA decreased the excitement and stereotypy in 3 of 9 rats, but did not decrease anorexia. These results suggest: 1) anterolateral but not anteromedial hypothalamic catecholaminergic (CA) neurons mediate the anorexic effect; 2) anterolateral and anteromedial CA neurons are involved in the excitement and stereotypy effects of d-amphetamine; 3) anorexia after d-amphetamine can be disassociated from

the excitement and stereotypy; and 4) stereotypy can be decreased without damaging the dopaminergic nigrostriatal pathway. (Author abstract)

182188 Dubinsky, B.; Robichaud, R. C.; Goldberg, M. E. Warner-Lambert Research Institute, Morris Plains, NJ 07950 **Effects of (-)delta9-trans-tetrahydrocannabinol in several animal models of aggression.** Federation Proceedings. 32(3):725, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the acute effects of (-)delta9-trans-tetrahydrocannabinol (THC) studied in several models of aggressive behavior were reported. Chlorpromazine was twice as active as THC in blocking isolation induced aggression in the mouse when each was tested 1 hr after administration. Doses of THC which produced taming did not impair rotarod performance, but chlorpromazine caused motor depression at doses below those which attenuated fighting. Inhibition of foot shock induced aggression in mice and rats by THC was considered to be related to the analgesic and/or motor depressant effects of the drug. THC did not block predatory aggression elicited by electrical stimulation of the hypothalamus in cats, but similar doses elevated the threshold current for stimulus bound hissing (emotional response) beyond the control range in other cats. These results indicate that THC has an antiaggressive profile which has properties in common with both tranquilizers and antidepressants. (Author abstract modified)

182189 Uyeno, Edward T. Stanford Research Institute, Menlo Park, CA 94025 **Effects of delta9-tetrahydrocannabinol on the dominance behavior of the rat.** Federation Proceedings. 32(3):725, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of delta9-tetrahydrocannabinol (THC) on the dominance behavior of the rat were reported. The time of peak effect experiment conducted 1,1.5, and 2 hrs after a single intraperitoneal administration of 0.5mg/kg of THC showed that the compound inhibited the dominance behavior of male Wistar rats in a food competition situation. The group tested 1.5hrs after the injection had the highest percentage of submissive experimental animals. A dose response study conducted at the time of peak effect showed that 0.25, 0.5, and 1mg/kg of THC inhibited considerably the dominance behavior in a dose related manner. An analysis of potency ratio showed that THC was significantly less potent than lysergic acid diethylamide in inhibiting the dominance behavior. (Author abstract modified)

182190 Miczek, Klaus A.; Gibbons, Judith L.; Barry, Herbert, III. Department of Psychology, Carnegie-Mellon University, Pittsburgh, PA 15213 **Effects of delta9-tetrahydrocannabinol and methysergide on defensive behavior in rats.** Federation Proceedings. 32(3):725, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the acute effects of delta9-trans-tetrahydrocannabinol (THC) studied in several models of aggressive behavior were reported. Chlorpromazine was twice as active as THC in blocking isolation induced aggression in the mouse when each was tested 1 hr after administration. Doses of THC which produced taming did not impair rotarod performance, but chlorpromazine caused motor depression at doses below those which attenuated fighting. Inhibition of foot shock induced aggression in mice and rats by THC was considered to be related to the analgesic and/or motor depressant effects of the drug. THC did not block predatory aggression elicited by electrical stimulation of the hypothalamus in cats, but similar doses elevated the threshold current for stimulus-bound hissing (emotional response) beyond the control range in other cats. These results indicated that THC has an antiaggressive profile which has properties in common with both tranquilizers and antidepressants. (Author abstract modified)

182191 Borgen, L. A.; Davis, W. M. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Delta9-tetrahydrocannabinol (delta9-THC) dose effects compared on three schedules of food-reinforced operant performance.** Federation Proceedings. 32(3):725, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, delta9-tetrahydrocannabinol (THC) dose effects were compared on three schedules of food reinforced operant performance. Although responding was depressed progressively with increasing doses under all schedules, significant differences were observed between the three schedules. FR response rates were most sensitive to THC, while VI performance was least sensitive. On the FI schedule only, low doses of THC produced a

moderate increase in response rate, while higher doses produced depression. At intermediate doses of THC, the overall response rate on FI schedule was reduced without alteration in the temporal pattern of performance. Under the FR schedule, postreinforcement pausing and running rates were equally sensitive to the effects of THC. (Author abstract modified)

182192 Pryor, G. T.; Mills, P. J.; Lydell, K. W.; Braude, M. C. Stanford Research Institute, Menlo Park, CA 94025 **Interaction of delta9-tetrahydrocannabinol (delta9-THC), caffeine, (C), nicotine (N), phenobarbital (P): effects on conditioned avoidance (CAR).** Federation Proceedings. 32(3):725, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the interaction of delta9-tetrahydrocannabinol (THC), caffeine (C), nicotine (N), and phenobarbital (P) in conditioned avoidance (CAR) was reported. Acutely, a dose of 10mg/kg THC slightly impaired performance, while a single injection of C, N, or P had only a slight or no effect at these doses. However, if N or P (but not C) were added to the acute dose of THC, performance was markedly impaired below that seen with each drug alone. Chronically, pretreatment with THC produced self-tolerance and attenuated the potentiating effects of N and P. Pretreatment with C, N, or P, respectively, either potentiated, had no effect, or attentuated the acute interactive effects with THC. These results together with those obtained using other testing procedures show that THC when taken with other widely used compounds may produce effects markedly different from those obtained when taken alone. (Author abstract modified)

182193 Ford, R. D.; Witt, Peter N.; Scarboro, Mabel B. North Carolina Department of Mental Health, Research Division, Raleigh, NC 27611 **Effects of single and repeated administration of water soluble 1-delta9-tetrahydrocannabinol (W-THC) on web-building of spiders.** Federation Proceedings. 32(3):725, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of single and repeated administration of water soluble 1-delta9-tetrahydrocannabinol (W-THC) on web building of spiders were reported. Only one application of 600 mg/kg THC produced a decrease in web building frequency and a change in the geometry of the lower part of the web, tending to make the normally oval shape more circular, without altering thread length or any other measures. When administration of the dose was repeated 10 times, once every other day, the effects persisted and increased: the few webs built were smaller and tended toward a circular shape. W-THC webs showed some resemblance to webs built after the application of strychnine. No significant development of tolerance to the drug effects on web building was detected. (Author abstract modified)

182194 Leander, J. David; McMillan, D. E. Department of Pharmacology, School of Medicine, University of North Carolina, Chapel Hill, NC 27514 **Substantial oral morphine intake by the rat using schedule-induced polydipsia.** Federation Proceedings. 32(3):726, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, substantial oral morphine intake by the rat using schedule induced polydipsia was reported. Initial exposure to various morphine solutions decreased drinking but increased lever pressing. After 2 weeks of exposure during daily 4 hr sessions to morphine solutions there was little change (as compared to the water solution) in average lever pressing rate; a slight dose dependent decrease in drinking rate; and an appreciable dose dependent increase in total dose consumed. The stable pattern of drinking exhibited by rats chronically maintained on a 0.5mg/ml solution was a tendency for drinking to no longer reliably be a postpellet phenomenon, but to be long drinks spaced throughout the 4 hr session. Thus, schedule induced polydipsia can be used to induce rats to chronically consume large doses of morphine orally. (Author abstract modified)

182195 Carney, J. University of Michigan Medical School, Ann Arbor, MI 48104 **Effects of morphine, codeine and naloxone on food- and codeine-reinforced responding in the rhesus monkey.** Federation Proceedings. 32(3):726, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the effects of morphine, codeine and naloxone on food and codeine reinforced responding in the rhesus monkey were reported. The rate of codeine reinforced responding was always lower than that of food reinforced responding and was inversely related to the dose of codeine infused. Food reinforced responding occurred at equal rates in periods I and III, a fact suggesting that

the negatively accelerated pattern of drug reinforced responding was not the result of a general depression of responding. Dose effect curves were repeated after more than 2 months of daily codeine self-administration. The dose effect curves for morphine and codeine on food reinforced responding were shifted to the right. Doses of morphine, codeine and naloxone, below those that reduced food reinforced rates, suppressed codeine reinforced responding. (Author abstract modified)

182208 Milloy, Svetlana; Glick, Stanley D. Mt. Sinai School of Medicine, New York, NY 10029 **Tolerance to the activity enhancing effects of d-amphetamine.** Federation Proceedings. 32(3):753, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, tolerance to the activity enhancing effects of d-amphetamine in mice was reported. Two groups of mice were used for each dose. Group I received daily saline injections for 7 days and on day 8 were placed in photocell activity boxes for a 30 minute session 15 minutes after being injected with d-amphetamine. Group II was tested daily for 8 days and received injections of d-amphetamine each day 15 minutes before being placed in the activity boxes. The dose response curves for both groups were found to have an inverted-U shape. The dose response curve for Group II was shifted to the right of the dose response curve for Group I. Since tolerance is usually defined as a shifting of the dose response curve to the right, it was concluded that tolerance to the stimulating effects of d-amphetamine had occurred. (Author abstract modified)

182209 Thornburg, John E. Department of Pharmacology, Michigan State University, East Lansing, MI 48823 **Relative importance of dopaminergic and noradrenergic neuronal systems for the stimulation of locomotor activity induced by amphetamine and other drugs.** Federation Proceedings. 32(3):753, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, the relative importance of dopaminergic and noradrenergic neuronal systems for the stimulation of locomotor activity induced by amphetamine and other drugs was reported. Alpha-methyltyrosine (MT), a tyrosine hydroxylase inhibitor, and U-14,624 (1-phenyl-3-(2-thiazolyl)-2-thioureal) or FLA-63 (bis(4-methyl-l-homopiperazinyl-thiocarbonyl disulfide)), inhibitors of dopamine-D-hydroxylase, were administered in the diet of mice for 4 hours prior to motor activity determinations in circular actophotometer cages. Intraperitoneal injections of d-amphetamine phenmetrazine, methylphenidate and pipradrol caused dose related increases in locomotor activity. The MT diet blocked the locomotor stimulant actions of d-amphetamine and phenmetrazine but not of methylphenidate or pipradrol. These results suggest that d-amphetamine and phenmetrazine exert locomotor stimulant effects through a dopaminergic mechanism. (Author abstract modified)

182210 Berger, Barry D.; Ritter, Sue; Wise, C. David; Stein, Larry. Wyeth Labs, Philadelphia, PA 19101 **Learning and memory after 6-hydroxydopamine (6OH-DA).** Federation Proceedings. 32(3):753, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, a study of learning and memory after 6-hydroxydopamine (6OHDA) was reported. The groups were tested first for acquisition of a simple spatial discrimination and reversal problem, then for learning in a more difficult visual discrimination task, and, finally, for retention of the visual problem after a 28 day forgetting interval. The spatial problems were learned rapidly and at the same rate by all groups. In the more difficult visual discrimination problem, animals that had been treated with 6OHDA in the lateral ventricle made significantly more errors in the early stages of acquisition than controls or animals in the 6OHDA group. Both 6OHDA groups exhibited deficits in the retention test. Norepinephrine levels in the diencephalon were reduced 59% in the lateral ventricle group and 48% in the aqueduct group. These observations are consistent with the idea that learning and memory are regulated by noradrenergic systems. (Author abstract modified)

05 TOXICOLOGY AND SIDE EFFECTS

175043 Sram, R. J.; Goetz, P.; Zudova, Z. Institut hygieny a epidemiologie, Prague, Czechoslovakia /**Genetic effects of LSD.**/ Geneticke ucinky LSD. Ceskoslovenska Psychiatrie (Praha). 69(2):80-87, 1973.

Mutation producing effects of LSD on Drosephila melanogaster, rat and mice were tested and evaluated. LSD was found to induce dominant lethal mutations in male mice if they were given

10-5000micrograms of LSD/kg, and in female mice if they were given 1000micrograms of LSD/kg. An interval of 3 months between LSD use and conception was recommended on complex estimation of possible ill effects on descendants so that the risk of transfer of serious damage to genetic material would be decreased. The use of LSD in pedopsychiatry and on healthy volunteers is regarded as questionnable, but further use of LSD in specific psychiatric indications is not considered objectionable. 59 references. (Author abstract modified)

176476 Ollerich, Dwayne A. Dept. of Anatomy, School of Medicine, University of North Dakota, Grand Forks, ND 58201 **Ultrastructure of CNS in lithium intoxication.** Final Report, NIMH Grant MH-18784, 1971, 38 p.

The ultrastructure of the central nervous system in lithium intoxication and the effects of lithium carbonate on the thyroid and kidney were studied. No unequivocal differences of ultrastructure were observed in the areas of the central nervous system that were surveyed. For studies of the thyroid, thyroid weights and values were greater in lithium-treated animals. A sex-related effect of lithium was indicated. Morphometric analysis revealed an increase in the mean diameter of sections of follicles and relative amounts of colloid, and a decrease in follicular cell heights in lithium-treated animals. The study of the effect of lithium carbonate on the structure of the rat kidney demonstrated that low dosages of lithium carbonate do affect the structure of the kidney. The 100mg/kg lithium dosage produced damage in all portions of the nephron. 56 references.

177097 Nakaguchi, Takeshi; Nomura, Masaji; Samejima, Kenji; Orita, Shigeru; Yokotan; Hajime; Takano, Kiichi. Takeda Research Laboratories, Osaka, Japan **Subacute toxicity of 8-chloro-6-phenyl-4H-s-triazolo(4,3-a) (1,4)-benzodiazepine (D-40TA) in male and female rats: oral administration for one month.** Journal of the Takeda Research Laboratories (Osaka). 32(2):158-171, 1973.

One month subacute toxicity of 8-chloro-6-phenyl-4H-s-triazolo (4,3-a) (1,4)-benzodiazepine (D-40TA) was examined in male and female rats at 10, 50, 200 and 500 mg/kg/day. A group treated by gum arabic solution, the vehicle, for gastric intubation, served as the control. At 400 and 200mg/kg/day D-40TA showed subacute toxicities in rats, inducing anemia and/or hypertrophy of the liver, cloudy swelling of the hepatic cells and enlargement of the stomach. At 50mg/kg or less, no significant toxicities were revealed in hematology, blood chemistry, urinalysis and histopathology, though a slight tolerance to the agent was developed during the daily treatments for one month. 8 references. (Author abstract modified)

177834 Rose, W. C.; Munson, A. E.; Bradley, S. G. Wistar Institute, 36th and Spruce Streets, Philadelphia, PA 19104 **Acute lethality for mice following administration of cyclophosphamide with barbiturates.** Proceedings of the Society for Experimental Biology and Medicine. 143(1):1-5, 1973.

The in vivo interaction between barbiturates and cyclophosphamide resulting in a rapid onset of death was investigated in mice. Although simultaneous administration of both compounds in BALB/c mice resulted in almost immediate fatality, when the drugs were given 1 hr apart the Ss survived. Pentobarbital lethality was potentiated in a parallel manner by 375mg cyclophosphamide/kg. Hexobarbital and phenobarbital successfully substituted for pentobarbital in eliciting enhanced lethality when administered with cyclophosphamide. Cyclophosphamide increased the duration of sedation elicited by each barbiturate. Pretreatment with multiple phenobarbital injections diminished the lethal action of subsequent challenge with cyclophosphamide and pentobarbital. However, Ss pretreated with phenobarbital were hyperactive to cyclophosphamide alone. The 9000g liver supernatant fraction derived from cyclophosphamide treated mice was about equal in metabolizing aminopyrine as was the 9000g liver supernatant fraction derived from normal mice. Cyclophosphamide had a minor effect on amount of pentobarbital recovered from mouse brain tissue 15 min after injection, compared to mice receiving pentobarbital alone. 13 references. (Author abstract)

178619 Cardauns, H.; Iffland, R. Institut fur Gerichtliche Medizin der Universitat D-5000 Koln 30, Melatatengurtel 60-62, FRG **/Fatal intoxication of a young drug addict with diazepam./** Uber eine todliche Diazepam (Valium) Vergiftung bei einem drogenabhangigen Jugendlichen. Archiv fur Toxikologie (Berlin). 31(2):147-151, 1973.

Fatal intoxication of a young drug addict with diazepam (Valium) is reported. The amount of the tranquilizer taken was estimated from the distribution of the drug and its demethylated

metabolite in body fluids, tissues, and organs. The toxic effect of diazepam in connection with other possible factors, such as alcohol and cooling, is also discussed. 10 references. (Author abstract)

179021 Blum. J. E.; Haefely, W.; Jalfre, M.; Polc, P.; Scharer, K. Abteilung fur Experimentelle Medizin der F. Hoffmann-La Roche & Co. AG, Basel, Switzerland **/Pharmacology and toxicology of the antiepileptic drug clonazepam./** Pharmakologie und Toxikologie des Antiepileptikums Clonazepam. Arzneimittel-Forschung (Aulendorf). 23(3):377-389, 1973.

Clonazepam (trade name Rivotril), an antiepileptic drug in the benzodiazepine family, with a broad spectrum of anticonvulsant activity in animals was studied. Investigations show that clonazepam: 1) protects mice from pentetrazole induced seizures; 2) is an antagonist of other systematically administered chemical convulsants; 3) prevents the propagation of electroencephalographic and clinical seizure activity from experimental epileptigenic foci; 4) elevates the threshold for electroshock seizure in mice and cats; 5) provides protection against photomyoclonic syndrome in the baboon; 6) suppresses the amygdalo hippocampally evoked potential in the cat; and 7) elevates the threshold for the generation of thalamic but not cortical after discharges. It has no effect on peripheral autonomic functions. Clonazepam shares with other benzodiazepines characteristic tranquilizing functions. Its broad antiepileptic spectrum of activity seems best explained by a potentiation of inhibitory mechanism in those subcortical brain structures which are responsible for the propagation of seizure activity. 30 references. (Journal abstract modified)

180056 Magour, S.; Coper, H.; Fahndrich, Ch. Institute of Neuropsychopharmacology, Free University, Berlin 19, Ulmenallee 30, Germany **Effect of chronic intoxication with (+)-amphetamine on its concentration in liver and brain and on (14C) leucine incorporation into microsomal and cytoplasmic proteins of rat liver.** Journal of Pharmacy and Pharmacology (London). 26(2):105-108, 1974.

Female Wistar rats were treated with increasing concentrations of (+)-amphetamine sulphate to determine the effect of chronic intoxication in the liver and brain and on microsomal and cytoplasmic proteins of rat liver. The concentrations of (3H) leucine incorporation into liver microsomal and cytoplasmic proteins was observed after 90 days of treatment with amphetamine. The relation between inhibition of microsomal protein synthesis and the increase of amphetamine concentrations in liver and brain is discussed. 13 references. (Author abstract modified)

181407 Wolf, Harold H. Ohio State University, Columbus, OH **Psychotropic drugs and phenotypical behaviors.** Psychopharmacology Bulletin. 10(1):73-74, 1974.

The effects of psychotropic drugs on genetically determined (phenotypical) and learned behavior patterns in several species are summarized. Results suggest that hereditary traits are less susceptible to modification than learned ones. Quantitative differences in behavior effects produced by chlorpromazine and other tranquilizers were found which could be used to distinguish the drugs from one another. Findings indicate that the degree to which early drug treatment alters adult behavior is influenced by the genetic background of the animals.

06 METHODS DEVELOPMENT

176763 Rajan, K. S. IIT Research Institute, 10 West 35th St., Chicago, IL 60616 **Metal chelation of chlorpromazines.** Final Report, NIMH Grant MH-22208, 1973, 32 p.

The metal chelation characteristics of 7-hydroxychlorpromazine and 7,8-dihydroxychlorpromazine and the unsubstituted chlorpromazine with magnesium(II), calcium(II) and copper(II) ions in the presence and in the absence of adenosinetriphosphate was investigated. The possible stabilization of these phenothiazines through metal chelation was also examined. A critical consideration of the pharmacological activities and metabolism of the phenothiazine group of tranquilizers indicates that a knowledge of their metal chelation characteristics is valuable for the proper understanding of the mechanism of their in vivo interactions with the catecholamines and the stabilization of the hydroxy isomers against the formation of toxic metabolites. 16 references. (Author abstract modified)

176867 Culver, Bruce; Norton, Stata. University of Kansas Medical Center, Kansas City, KS 66103 **A method for analyzing CNS effects of drugs and brain lesions on permanent groups of rats.** Federation Proceedings. 32(3):818, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, a method for analyzing CNS effects of drugs and brain lesions on permanent groups of rats was reported. It was hypothesized that control of the stimulus level of the environment in which animals live can be used to enhance responses to various CNS insults. Administration of morphine SO4 and d-amphetamine HCl, carbon monoxide ecposure, and thalamic lesions all produced hyperactivity but the amount of activity varied depending on duration of lighting, the number of rats in the multi runway living cage, and introduction of a strange rat. This technique shows promise as a sensitive method for analyzing some new effects on behavior. (Author abstract modified)

177735 Wolff, B. Berthold. Department of Medicine, New York University Medical Center, 550 First Avenue, New York, NY 10016 **Evaluation of hypnotics in outpatients with insomnia using a questionnaire and a self-rating technique.** Clinical Pharmacology and Therapeutics. 15(2):130-140, 1974.

A brief, forced choice daily questionnaire was developed to quantitatively evaluate the efficacy of hypnotics over an extended period in outpatients with insomnia. The usefulness of this questionnaire, combined with the patients' ranking of successive weeks, was tested in two studies. The first, involving 44 patients during 3 weeks, used a relatively potent hypnotic, 100 mg sodium pentobarbital, while the second, involving 36 patients during 4 weeks, used a mild hypnotic, two Excedrin-PM tablets. Both studies indicated the two subjective measures to be appropriate; the potent and the mild hypnotic were significantly discriminated from placebo under double-blind conditions. The first study also included a magnetic pillow insert that was not differentiated from a placebo pillow insert, but that, nevertheless, appeared to have some central nervous system effects related to a greater frequency and more vividness of recall of dreams. It was concluded that these subjective measures are valuable for chronic hypnotic assays under normal (i.e.,home) conditions where more objective laboratory techniques are not applicable. 19 references. (Author abstract)

178948 Mallach, H. J.; Moosmayer, A.; Rupp, J. M. Institut fur Gerichtliche Medizin, Universitat Tubingen, Tabingen, Germany /**Gas chromatographic analysis of benzodiazepines. Part I: Medazepam and its metabolites.**/ Zur gaschromatographischen Analytik der Benzodiazepine. 1. Mitteilung: Medazepam und seine Metabolite. Arzneimittel-Forschung (Aulendorf). 23(4):614-616, 1973

A gas chromatographic method using a nitrogen specific flame ionization detector, which completely separates medazepam and its major metabolites is described. Serum and urine extraction and quantitative determination are described and regression lines and standard deviations calculated. Sensitivity limits are of the order of 2.5to 20ng/ml when 4ml serum or urine are extracted. Blood level curves were recorded following a 30mg oral dose of medazepam with and without alcohol load. Resorption was rapid, the test without alcohol load showing a higher medazepam concentration of approximately 656ng/ml after 40 min, with alcohol load 1037ng/ml serum after 100 min. 9 references.

180055 Tuomisto, Jouko. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10, 00170 Helsinki, Finland **A new modification for studying 5-HT uptake by blood platelets: a re-evaluation of tricyclic antidepressants as uptake inhibitors.** Journal of Pharmacy and Pharmacology (London). 26(2):92-100, 1974.

The effect of imipramine and other antidepressive drugs on 5-HT uptake by rabbit platelets was reevaluated. Imipramine causes a half maximal inhibition at .1micromole or lower concentration. Other tricyclic drugs and phenothiazine derivatives are much more effective than previously demonstrated. The correlation of uptake inhibition in platelets with 5-HT uptake inhibition in brain synaptosomes is found to be highly significant. When the technique is modified, the level of uptake inhibiting potency in an absolute sense is close to that described for other tissues, especially brain synaptosomes. Platelets can more reliably be used as an easily obtainable model for nerve endings. 36 references. (Author abstract modified)

180537 no author. no address **Solubilization and purification of brain RNA polymerase.** Final Report, NIMH Grant MH-20549, 1972, 2 p.

A method was developed for the quantitative solubilization of deoxyribonucleic acid (DNA) dependent ribonucleic acid (RNA) polymerase from whole brain nuclei of rat liver, and purification of

the solubilized enzyme. Over 90% of the activity originally present in the intact nuclei was recovered. The technique is reviewed. (Author abstract modified)

181653 Matsushita, Kensuke; Kawano, Kazunari; Kojo, Jiro; Matsumoto, Kei. Department of Neuropsychiatry, Faculty of Medicine, Kagoshima University, Japan **Direct determination of lithium in serum by atomic absorption spectroscopy.** Kyushu Neuro-psychiatry (Fukuoka). 19(2):136-146, 1973.

A direct method for the determination of lithium in serum by atomic absorption spectroscopy is described, employing 5% trichloroacetic acid as a diluent and a deproteinizing agent. The new method is simple and sufficiently reliable for clinical purposes. 6 references. (Author abstract)

182178 Heldman, J.; Naftchi, N. E. Laboratory of Biochemical Pharmacology, NYU Medical Center, New York, NY 10016 A **sensitive, simple method for measurement of tyrosine hydroxylase and tryptophan-5-hydroxylase activities.** Federation Proceedings. 32(3):707, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, a rapid and simple method for the analysis of tyrosine hydroxylase (TH) and tryptophan-5-hydroxylase (HTPase) was reported. It is based on the formation of very stable, insoluble complexes of potassium dichromate with the respective products of TH and HTPase reactions: L-3,4-dihydroxyphenylalanine (dopa) and 5-hydroxytryptophan (5-HTP). 14C-tyrosine (tyr) and 14C-tryptophan (tryp), the substrates, do not react with dichromate to form complexes. After termination of the enzyme reactions with TCA and centrifugation to discard the enzyme protein, dichromate is added, together with carrier product. Carrier tyr and tryp are also added to minimize coprecipitation of the labeled substrates. The insoluble complex is pelleted by centrifugation and washed several times with dilute HCl and water. The complex is then brought into solution with concentrated nitric acid and counted in a liquid scintillation spectrometer in Aquasol. With the use of saturating levels of tyr and tryp, the reaction with the respective enzymes is linear with respect to both time and enzyme concentrations. (Author abstract modified)

182203 Cho, A. K.; Lindeke, B.; Sum, C. UCLA School of Medicine, Los Angeles, CA 90024 A **gas chromatographic method for the quantitative estimation of N-hydroxyphentermine.** Federation Proceedings. 32(3):734, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, a gas chromatographic method for the quantitative determination of N-hydroxyphentermine (2-methyl-1-phenylisopropylhydroxylamine) developed with phenylacetone oxime as the internal standard was reported. In studies with rabbit liver preparations, incubation mixtures were extracted with 3% isopropanol in petroleum ether containing phenylacetone oxime. The solvent was evaporated under N2 and the residue derivatized and chromatographed. By use of this procedure the properties of this aliphatic amine N-hydroxylation reaction were examined. Phenylethylamine, amphetamine, and p-chlorophentermine were also converted to their hydroxylamine derivatives by these preparations. (Author abstract modified)

CLINICAL PSYCHOPHARMACOLOGY

07 EARLY CLINICAL DRUG TRIALS

175282 Khorramzadeh, E.; Lotfy, A. O. Pahlavi University School of Medicine, Shiraz, Iran **The use of Ketamine in psychiatry.** Psychosomatics. 14(6):344-346, 1973.

The abreactive properties of Ketamine hydrochloride were investigated in 100 patients of a psychiatric unit of a hospital in southern Iran. Abreactive effects were summarized as 1) excitement, 2) emotional discharge, 3) verbalization of conflict, and 4) emergence phenomenon. Ketamine at 0.4to 0.6mg/kg bodyweight led to minimal anesthetic effect and the abreactive response in nearly all of the subjects. Ketamine was found to be a fast acting drug with a short duration of action. It induced regression, introversion, lability of mood and perceptual disturbances. It activated unconscious and repressed memories, reviving past traumatic events with intense emotional reaction. Patients showed a good degree of verbosity and inhibitions were gone. A followup 1 year later showed most patients doing well, though two required a further injection. Side-effects were minimal. 6 references.

177319 Ota, K. Y.; Kurland, A. A.; Slotnick, V. B. Spring Grove State Hospital, Baltimore, MD **Safety evaluation of penfluridol, a new long-acting oral antipsychotic agent.** Journal of Clinical Pharmacology. 14(4):202-209, 1974.

The safety and effectiveness of penfluridol in controlling the psychiatric symptomatology of 12 chronic psychotic patients was studied. Administered orally once a week at starting doses of 5 to 10mg with final maximum doses of 160 or 200mg, the drug had no clinically significant effect on vital signs or laboratory test results and adverse side reactions were no more frequent than in controls using neuroleptic medications. Extrapyramidal reactions occurred only rarely and then usually only at doses of 100mg or more, considerably above the therapeutically effective dosage range of 60 to 80mg. On the Brief Psychiatric Rating Scale, the Nurses' Observation Scale for Inpatient Evaluation, and a Clinical Global Impression scale, penfluridol was at least as effective as the conventional phenothiazines received by the control group. In light of the advantages of an oral drug effective for 1 week following a single dose, further clinical study of penfluridol is definitely warranted. 10 references. (Author abstract)

177747 Roth, Thomas; Kramer, Milton; Schwartz, John L. Department of Psychiatry, College of Medicine, University of Cincinnati, Cincinnati, OH **Triazolam: a sleep laboratory study of a new benzodiazepine hypnotic.** Current Therapeutic Research. 16(2):117-123, 1974.

Experiments demonstrating triazolam to be a potentially effective and safe hypnotic are presented. In normal young male subjects, in doses of 0.25 to 1.0mg.,triazolam was successful in rapidly inducing and effectively maintaining sleep without disrupting, in important ways, the architecture of sleep. Triazolam, when used for three nights, did not lead to significant subjective complaints or any deterioration in the physical condition of the subjects. Examination of the effect of triazolam in the sleep laboratory on insomniacs in both acute and chronic trials and in clinical trials is warranted. 2 references. (Author abstract)

180722 Eymard, P.; Werbenec, J.-P. Centre de Recherches et d'Etudes Pharmacologiques, 26, rue Prosper-Merimee, 38-Grenoble, France **/Complemental pharmacological study of di-N-propylacetamide or depamide/.** Etude pharmacologique complementaire du Di-n-propylacetamide ou Depamide. Therapie (Paris). 27(1):11-24, 1972.

An assessment of the administration of di-N-propylacetamide (Depamide) in humans on anxiety, aggressiveness, and more generally in the field of normalization of behavior is presented. Depamide is no longer considered a neuroleptic, but a member of the minor tranquilizer category. Results reveal antiulcerus, anxiolytic, antiaggressive, antiamphetaminic properties, and to a certain extent, antireserpinic properties. It is suggested that due to these results, Depamide does not belong to a definite pharmacological category. Depamide is defined as a thymic regulator in human applications. 8 references. (Author abstract modified)

180725 Deniker, P.; Peron-Magnan, P.; Ginestet, D.; Loo, H.; Colonna, L. 1, rue Cabanis, Paris, 14 **/Preliminary studies of carpipramine: a compound similar to both antidepressants and neuroleptics./**

Essais preliminaires de la carpipramine: compose apparente aux antidepresseurs et aux neuroleptiques. Therapie (Paris). 27(1):177-181, 1972.

A preliminary study of the effects of carpipramine on 40 schizophrenics and toxic psychotics is discussed. Investigation reveals that chemically, carpipramine has a tricyclic nucleus similar to imipramine, but with a butyrophenone like side chain. Results show that the compound acts against severe target symptoms found in a number of cases, particularly in autism, catatonic syndromes, hebephrenia and toxic psychoses. Its activity on the other psychotic symptoms is low. It is suggested that these observations show an original action against important symptoms usually unresponsive to chemotherapy. (Author abstract modified)

181771 Namiki, Masayoshi; Kawakami, Kiyoshi; Hasegawa, Naoyoshi; Suzuki, Jinichi; Higuchi, Masamoto; Ueno, Masamitsu; Nakano, Shigeyuki; Tanaka, Masatoshi. Hokkaido University School of Medicine, Japan **A clinical evaluation of a new anxiolytic drug (thienodiazepine derivative Y-6047) in neurotics and psychosomatic disorders -- a preliminary report.** Journal of Japanese Psychosomatic Society (Tokyo). 13(3):180-186, 1973.

The effect of Y-6047 on neurosis and psychosomatic diseases was studied in 25 patients with neurosis, 2 with masked depression and 44 with psychosomatic disease treated with Y-6047 (6-40mg/day, for 3-28 days, orally). The drug was remarkably effective in 16 patients whose symptoms almost completely disappeared and who had no problems in living a normal daily life, effective in 44 patients whose symptoms improved but could not live normally and was slightly effective in 16 patients. This drug was effective on anxiety, tension, irritation, fatigue, and digestive and circulatory organ disturbances. It was most effective at a dose of 30mg/day, however, its effects were perceptible at the minimum dose of 6mg/day. Effects appeared within 2-7 days after the beginning of treatment. Minor side-effects, such as drowsiness in one patient, headache in one and dizziness in one were observed. 3 references.

08 DRUG TRIALS IN SCHIZOPHRENIA

175119 Tanimukai, Hiroshi; Inui, Masashi; Takahashi, Hisatake; Kaneko, Ziro. Department of Psychiatry, Osaka University School of Medicine, Japan **A double-blind comparison of clozapine with thioridazine on schizophrenia.** Clinical Psychiatry (Tokyo). 15(3):269-284, 1973.

The effects of clozapine (C) and thioridazine (T) on schizophrenia are compared, based on a double-blind study. Patients, 15 to 55 years old, who had not been treated with any psychotropic drugs for 1 week, were treated with T (60 to 720mg/day for 10 weeks), or with C (50 to 600mg/day for 10 weeks). C was slightly more effective in the total sample, particularly in catatonic schizophrenia. T was superior in delusional schizophrenia. Both exhibited strong effects on psychomotor excitation, with T showing exemplary effects on stupor. Clozapine caused side-effects in most patients though rarely severe enough to cease treatment. Thioridazine caused side-effects in two thirds of the sample, none serious. 25 references.

175460 Bagadia, V. N.; Doshi, S. U.; Hebbar, Y. V.; Chawla, R.; Saraf, K. R.; Shah, L. P.; Sheth, U. K. Psychiatric Department, K.E.M. Hospital, Bombay 12, India **Flupenthixol in schizophrenia.** Indian Journal of Psychiatry (Madurai). 14(1):24-30, 1972.

A clinical trial of 9 new thioxanthine drug, Flupenthixol, carried out in 145 cases of schizophrenia, is reported. Almost half of the patients showed improvement from moderate to complete recovery. The drug was found most useful in quiet and drive deficit schizophrenics, and in the catatonic type, but it was not found useful for any particular symptoms or prognosis types. 4 references. (Author abstract modified)

175550 Inanaga, Kazutoyo; Oshima, Masachika; Tachibana, Hisayuki. Dept. of Neuropsychiatry, Kurume University School of Medicine, Kurume, Japan **Three cases of schizophrenia treated with L-dopa.** Kurume Medical Journal (Kurume). 18(3):161-168, 1971.

Three cases of schizophrenia are discussed in which remarkable recovery followed treatment with L-dopa and major tranquilizers. Patients had not responded to treatment with tranquilizers alone. Tentative dosage of L-dopa was 400 to 1200mg per day. Hallucination and thought disorder disappeared as well as apathy and lack of spontaneity. In one case, the symptoms reappeared when another antiparkinsonian drug was used instead of L-dopa. It is concluded that continuous administration of L-Dopa is necessary for the improvement of symptoms. 16 references. (Author abstract modified)

175725 Frost, Monica. no address **Acute schizophrenia.** Health and Social Service Journal (London). 84(4373):296-297, 1974.

The combination of drugs and domiciliary care are discussed regarding the treatment of acute schizophrenia. It is felt that with suitable medication, schizophrenic patients generally can be managed on an open ward without the stigma of certification and compulsory admission. Drugs for hospitalized and outpatients are also discussed. The trend to avoid labelling is discussed and the symptoms of simple, catatonic, hebephrenic and paranoid schizophrenia are described. Physical methods of treatment, both modern and centuries old, are presented.

176446 Maramis, W. F.; Prasadio, Triman. Department of Neurology and Psychiatry, Faculty of Medicine, University of Airlangga, Surabaya, Indonesia **/Clinical trial of Perazine (Taxilan) in treatment of schizophrenia./** Percobaan klinik terhadap Perazine (Taxilan) dalam pengobatan schizophrenia./ Indonesian Psychiatric Quarterly (Djakarta). 6(3):75-82, 1973.

Clinical trials of Perazine (taxilan) in treating schizophrenia are discussed. Results of tests conducted on patients diagnosed as schizophrenic upon entrance to the psychiatric department at Airlangga University over a 9-month period are discussed. Of a total of 77 diagnosed, 60 were treated with Perazine. The group consisted of 36 females and 24 males, between 13 and 63 years of age. The patients were divided into two groups, those ill over 6 months and those who had been ill less than 6 months, and beginning dosage was 300 to 900mg daily. Optimum daily dose was 900 to 1200mg, all in tablet form. Each patient was checked twice a week on a scale of 1 to 4, against a list of 21 symptoms. A final check on a scale of 1 to 6 was made at the end of the fourth week. The level of improvement in both groups is tabulated, indicating that the under 6 months group responded better to the treatment. Results by type of schizophrenia and the average rate of improvement overall compared with two other medications are provided, as is the average decrease in symptoms for both groups, the side-effects found, and the number of patients affected. 7 references.

176447 Deguchi, Tetsuya. Jieitai Chuo Hospital, Japan **Experience in the application of diceplon (APY-606) -- compared with floropipamide.** Medical Consultation and New Remedies (Tokyo). 8(11):119-123, 1971.

The effect of diceplon (APY-606) on general schizophrenic symptoms is compared with that of floropipamide (FL). Seventeen 21-to 46-year-old schizophrenic patients treated with FL (150 to 300mg/day) combined with perazine, chlorpromazine, levomepromazine or perphenazine for 4 to 51 months had FL replaced with diceplon for 21 days. Diceplon matched the performance of FL in most patients and was shown superior to FL in one case. No side-effect on blood pressure, blood, liver or kidney was observed. Although APY-606 does not have exactly the same effect as FL, it has a similarly good effect.

176467 Nagai, Tetsu; Iwasawa, Kiyoshi; Iwajima, Yutaka. Mikatahara Hospital, Japan **Clinical effect of a new psychotropic drug, Zisepron, in treatment of psychiatric diseases in comparison with thioridazine.** Medical Consultation and New Remedies (Tokyo). 8(8):169-176, 1971.

The effect of Zisepron (Zp) on general psychiatric symptoms was compared with that of thioridazine (Th) in 19 predominantly schizophrenic patients treated with Th (75 to 450mg/day), with 33% of Th replaced by Zp in week one, 66% in week two, and all of Th replaced by Zp during the third week. Among the 19 patients, 58% showed improvement in symptoms and attitude in the 3rd week. An additional 26% showed further improvement after treatment with Zp alone for 3 weeks after cessation of Th. Improvements noted were in the areas of volition, behavior, language, thinking, awareness of illness, interpersonal relationship, recreation and exercise, daily life habits and work. No side-effect due to Zp was identified. These results indicate that Zp is compatible or superior to Th in its effect on general psychiatric symptoms and attitude of psychiatric patients. 11 references.

176468 Saito, Norihiko; Inada, Hiroshi; Saito, Kazuharu; Mita, Toshio. Iwate Medical College, Japan **Experience in the application of a new drug, DP-181 (oxypertine), in treatment of schizophrenia.** Medical Consultation and New Remedies (Tokyo). 8(9):173-180, 1971.

The effect of DP-181 (oxypertine) on schizophrenic symptoms was studied in 46 15- to 61-year-old schizophrenic patients orally treated with this drug (60 to 300mg/day) for 1 week to 6.5months. The results show that among the 46 patients the drug was effective in more than half. The drug was maximally effective on autism and

lack of volition. The maximum effect was observed within 2 to 4 weeks after the beginning of treatment in those patients treated with 120 to 180mg/day. Side-effects of insomnia, tremor, irritation, nausea, dizziness and salivation were observed but were generally controllable with anti-Parkinsonians or sleeping pills. 10 references.

176469 Ishikawa, Tetsuo. National Konodai Hospital, Japan **Examination of the methods of using fluphenazine enanthate.** Medical Consultation and New Remedies (Tokyo). 8(9):165-172, 1971.

The effect of fluphenazine enanthate on schizophrenic symptoms was studied in 28 patients treated intramuscularly with this drug (12.5to 50mg) once in 2 weeks for 11 times with or without treatment with other drugs. Among 10 patients treated solely with this drug, 6 showed improvement. Among 18 patients treated with this drug and another drug at the same time, 12 showed improvement. Single treatment with this drug was effective in improving volition and behavior, but not very effective on thinking and emotion. Combined treatment was effective in all the above aspects. Side-effects, such as dyskinesia, Parkinsonism, akathisia, insomnia, were induced by single treatment but were easily controlled by treatment with anti-Parkinsonism agents. 7 references.

176470 Tanaka, Kunio; Tonami, Munetoku; Yoshida, Sumihiko; Miyamoto, Kunio; Okumura, Yukio; Kimura, Shigeki; Itonaga, Yoshiaki. Fukuoka Prefectural Dadaifu Hospital, Japan **Clinical effects of diceplon, a psychotropic drug.** Medical Consultation and New Remedies (Tokyo). 8(11):125-130, 1971.

The effect of deceplon on psychiatric illness was studied in 20 chronic patients (mainly schizophrenic) and 4 acute psychotic patients, several with organic etiology, treated with this drug (100 to 450mg/day) for 16 to 60 days with or without other psychotropic drugs which were previously used for treatment. Deceplon was effective in acute psychosis, moderating delusion, hallucination, suicidal desire, and awareness of illness. Side-effects were observed in all four Ss, but resulted in termination in only one. The drug was useful in only 20% of the chronic Ss, showing no effect in 60%. Minor side-effects were observed but resulted in no terminations. 3 references.

176472 Arioka, Iwao; Ohmi, Sakuo; Nishimura, Kimihiro; Asao, Yukihiko; Inamori, Jiro; Katsuyama, Nobufusa; Tanaka, Yoshi; Adachi, Kohichi; Inoue, Kazunori. Nara Prefectural Medical College, Japan **Experience in the use of a low dosage of carpipramine (Defekton).** Medical Consultation and New Remedies (Tokyo). 8(10):199-203, 1971.

The effect of low dosages of carpipramine (Defekton) on psychiatric symptoms was studied in twenty-four 27- to 56-year-old patients, mainly schizophrenics, orally treated with this drug (30 to 60mg/day) in addition to those drugs currently used in controlling these patients in a less than effective way. Carpipramine was effective on lack of volition and dull emotion in five schizophrenic patients, but generally had little or negative effect on the majority of Ss. 18 references.

176541 Ara, Tadashi. Iwaya Hospital, Japan **Clinical application of APY-606.** Medical Consultation and New Remedies (Tokyo). 8(11):133-140, 1971.

The effect of diceplon (APY-606) on schizophrenia was studied in 17 20 to 57-year-old schizophrenic patients treated with APY-606 (150 to 350mg/day) for 10 to 150 days, combined with various previously applied psychotropic drugs. This drug induced remarkable to moderate improvement in facial expression, behavior and interpersonal relationships in seven patients, no improvement in nine and slight aggravation in one. No significant side-effects were observed, except for sleepiness in one patient. Although this drug was not effective in eliminating hallucination or delusion and did not induce dramatic improvement in general symptoms, it is useful in inducing a favorable state in patients for psychotherapy and milieu therapy.

176673 Gardos, George; Orzack, Maressa Hecht; Finn, Geraldine; Cole, Jonathan O. Boston State Hospital, 591 Morton Street, Boston, MA 02124 **High and low dose thiothixene treatment in chronic schizophrenia.** Diseases of the Nervous System. 35(2):53-58, 1974.

The characteristics of chronic schizophrenics who respond well to low dose thiothixene treatment were investigated. Forty hospitalized treatment resistant schizophrenics were randomly assigned to high (40mg) or low (10mg) daily oral doses of thiothixene. Differential effects were predicted on measures of central nervous system

(CNS) arousal, performance tests, clinical ratings, and perceptual - cognitive training. The high dose showed effects consistent with antipsychotic activity. The low dose showed some changes indicating activating properties. Side-effects on high dose included several instances of EPS: akathisia, tremor and transient CNS stimulation. Low dose produced persistent CNS stimulation: excitement and insomnia. The differentiation of 'turbulence' from 'activation' is of clinical importance. It is concluded that methodological problems of sample size, lost performance, and electroencephalogram data, fixed dose level, and refractory patients probably account for the paucity of statistically significant dose differences. 31 references. (Author abstract)

176722 Sakurai, Tsunao; Nakazawa, Yoichi; Saito, Masa; Sameshima, Takashi; Maeda, Hisao; Kamachi, Kiichiro; Yamauchi, Masumi. Department of Neuropsychiatry, Faculty of Medicine, Kyushu University, Japan **Clinical study of DP 181 (Oxypertine).** Kyushu Neuro-psychiatry (Fukuoka). 15(2):261-265, 1969.

Effects of DP 181 (oxypertine) on schizophrenia were studied in 42 Ss, 18 to 59 years old, orally treated with DP 181 (increasing doses from 60mg to 360mg/day) for 10 to 20 weeks. The results show: the drug was effective in 9 patients, slightly effective in 11, and noneffective or harmful in the others. The drug improved retardation and withdrawal symptoms, but did not show much effect on hallucination and delusion. Minor side-effects, such as insomnia, irritability and tremor of fingers and muscle rigidity were noted in most patients. These side-effects disappeared through administration of sleeping pills and anti-Parkinsonism agents. (Author abstract modified)

176726 Takashina, Kenji; Toraiwa, Shigemichi; Hayakawa, Junko. Tohokukai Hospital, Japan **Clinical experiences with navane in chronic schizophrenia.** Medical Consultation and New Remedies (Tokyo). 9(9):1955-1963, 1972.

Clinical experience with the use of Navane (Thiothixene) on 33 patients with chronic schizophrenia are reported and tabulated by age and sex, age at onset, number of recurrences, date of most recent onset, total number of diagnoses, dosage, other medication, length of time on maintenance, principal symptoms prior to treatment, change in symptoms, evaluation, and side-effects. Efficacy was 54.5% when dosage was 60 to 140mg daily, decreasing to 27% for 10 to 40mg daily. Improvement was noted within 3 weeks, and efficacy was high when dosage was 60mg daily. Spontaneity increased, general condition and conduct improved, and there was a gradual improvement in composure in some cases, with great changes found in the general physical state. Side-effects were easily controllable.

176727 Shiozaki, Masakatsu; Aso, Shigeko. Aiseikai Aisei Hospital, Japan **Clinical experiences with a psychotropic drug (oxypertine) in chronic schizophrenia.** Medical Consultation and New Remedies (Tokyo). 9(9):1977-1985, 1972.

Clinical experience with oxypertine, a psychotropic drug, in chronic schizophrenia is discussed. Results are tabulated along with age, sex, daily dosage, number of days of medication, duration of illness, other medication used simultaneously, symptoms prior to treatment, change after administration of medication, and side-effects. Degree of improvement is cited in terms of duration of illness prior to treatment, and side-effects are classified. Eighteen out of 30 patients showed improvement after treatment, a 60% effectiveness result, but improvement was slow, extending over 4 to 6 weeks in some cases. Improvement was most marked in patients suffering from spontaneous lack of will, apathy, facilitation deficiency, and refusal symptoms. Greatest effectiveness was found when more than moderate dosage was prescribed.

177568 Mori, Atsutoshi. Toho University, Department of Medicine, Japan **Experience in the use of FK-880 (sulpiride) in the field of psychiatry.** Medical Consultation and New Remedies (Tokyo). 8(4):105-113, 1971.

The effects of FK-880 (sulpiride) on mental disturbances based on experimental administration of this drug to 35 patients with schizophrenia, two with atypical psychosis, three with neurosis, and one with senile psychosis were studied. The drug showed various effectiveness in different patients. Seventy percent of the patients showed improvement within 2 weeks after the beginning of treatment. The drug was effective in cases of hallucination, delusion, anxiety tension, and depression. Side-effects were observed in 12 patients, including tremor, Parkinsonism, insomnia and fatigue. 10 references.

177669 Rosenthal, Randall; Bigelow, Llewellyn B. NIMH, Saint Elizabeths Hospital, Washington,

DC 20032 **The effects of physostigmine in phenothiazine resistant chronic schizophrenic patients: preliminary observations.** Comprehensive Psychiatry. 14(6):489-494, 1973.

The effects of physostigmine in phenothiazine resistant chronic schizophrenics were studied. Five chronic schizophrenic patients were given varying dose schedules of oral physostigmine in addition to their maintenance phenothiazine medications. Marked but transient clinical improvement was seen in all five patients. The time course of the latency and improvement periods seemed to be dependent upon the dose schedule of physostigmine. 11 references.

177748 Rada, Richard T.; Donlon, Patrick T. Department of Psychiatry, School of Medicine, University of New Mexico, Albuquerque, NM **Piperacetazine in ambulatory chronic schizophrenic patients.** Current Therapeutic Research. 16(2):124-129, 1974.

The effectiveness of piperacetazine in 16 of 18 outpatient chronic schizophrenic patients who completed the 14 week study period was demonstrated. Piperacetazine in dosage higher than previously recommended was effective with seven of eight patients who had minimal symptomatic improvement on a brief trial of standard dose. Although side-effects were higher in patients receiving high dosage, liver toxicity was less in high dose recipients. It was suggested that piperacetazine may have a differential anxiolytic action and may also be effective in schizophrenics with a depressive component. 8 references. (Author abstract modified)

177754 Engelhardt, David M.; Polizos, Polizoes; Waizer, Jonas; Hoffman, Stanley P. Dept. of Psychiatry, State Univ. of New York, Downstate Medical Center, 450 Clarkson Ave., Brooklyn, NY 11203 **A double-blind comparison of fluphenazine and haloperidol in outpatient schizophrenic children.** Journal of Autism and Childhood Schizophrenia. 3(2):128-137, 1973.

A double-blind comparison of fluphenazine and haloperidol in outpatient schizophrenic children is presented. Ss were 30 schizophrenic children, 6 to 12 years old. The duration of treatment was 12 weeks. Mean dosage for both treatment groups was 10.4mg/d, with a maximum dose of 16 mg/d. Both fluphenazine and haloperidol proved highly effective in the population of schizophrenic children, with the two drugs indistinguishable in overall efficacy. Both drugs were characterized by low incidence of side-effects with a tendency for fluphenazine treatment to induce extrapyramidal symptoms with greater frequency than haloperidol. Side-effects were easily managed by dose reduction or contramedication. No child had to be terminated due to an adverse reaction. It is suggested that these findings, as well as other reports in literature, indicate that fluphenazine and haloperidol deserve consideration in the treatment of schizophrenic children. 15 references. (Author abstract)

177818 Bigelow, Llewellyn B. Laboratory of Clinical Psychopharmacology, Division of Special Mental Health Research, IR, NIMH, Saint Elizabeth's Hospital, Washington, DC **Effects of aqueous pineal extract in chronic schizophrenia.** Biological Psychiatry. 8(1):5-15, 1974.

Ten young chronic schizophrenic patients were given daily intramuscular injections of either aqueous pineal extract or of placebo in a double-blind clinical study in which each patient served as his own control. Previous reports have stated that extracts of beef pineal glands have therapeutic value in schizophrenia. In this study, the degree of psychosis as measured by a nurses' rating scale was reduced significantly in five of 10 patients. When all 10 patients were considered as a group, extract treatment was superior to placebo. The degree of improvement in most cases was modest or consisted of accelerating an apparent trend to improvement. Since the material given is derived from a biological source, these results may offer a clue to the etiology of some forms of schizophrenia. 7 references. (Author abstract modified)

177994 Ito, Sei. Keio Gijiku University, Japan **Schizophrenia.** Nippon Rinsho (Osaka). 28(Special Issue):142-143, 1970.

Types of psychotropic drugs applicable to schizophrenia and their effects are discussed. Types of psychotropic drugs for schizophrenia, appropriate dosage and side-effects are considered. The brief history of the development of the psychopharmacology of schizophrenia is also discussed. 5 references.

178021 Makihara, Hiroshi; Usui, Hiroshi; Sugiyama, Kazu; Suetsugu, Tetsuro; Kato, Masatake; Nagajima, Masanori; Ishikawa, Takako. Department of Neuropsychiatry, Nihon University School of Medicine, Japan **Clinical ex-**

perience with fluphenazine enanthate. Medical Consultation and New Remedies (Tokyo). 9(3):623-631, 1972.

The effects of fluphenazine enanthate on schizophrenia were examined in 31 Ss, aged 19 to 52 years. Various dosages were tried as well as concurrent treatment with other drugs, including perphenazine, trifluprornazine, levomepromazine, promethazine, trihexyphenidyl hydrochloride and chlorpromazine. The drug was effective in 61% of the patients. Severe side-effects were noted in two cases, but were controlled with other psychotropic drugs. 9 references.

178053 Yauchi, Nobuo; Gamaike, Naohiro; Ota, Hiroshi; Tanaka, Tetsu. Minami Ogura Hospital, Japan **Comparison of the effects of Y-4153 and carpipramine on schizophrenia by a double-blind method.** Medical Consultation and New Remedies (Tokyo). 9(4):853-869, 1972.

Forty schizophrenic patients and one patient with obsessive-compulsive neurosis are discussed as part of clinical tests to establish the efficacy of Carpipramine (Defekton, CPP) as compared to results obtained using Y-4153 (Clocaprimine). CPP was administered in doses of 90 to 300mg for from 14 to 98 days. The drug was effective in 47% of the cases. No change was noted in 26.5%, and 26.5% worsened. Patients' feelings were enhanced during the first stage, beginning on the fifth to seventh day. Patients improved or worsened during the second stage, at about 5 weeks. Treatment was most effective in cases of chronic schizophrenia, less effective in cases of hebophrenia, other schizophrenic types, and obsessive-compulsive neurosis. Results are tabulated by age, sex, type of disease, symptoms prior to tests, prior medication, dosage, progress after one month, evaluation, progress from first to second month, and side-effects. Extrapyramidal effects were not noted. Improvement in social attitude and use of words was great. 4 references.

178187 Jus, A.; Jus, K.; Gautier, J.; Villeneuve, A.; Pires, P.; Lachance, R.; Villeneuve, R. Department de recherches, Hopital St.-Michel-Archange, Quebec 5, Canada /**Dream reports after reserpine administration in chronic lobotomized schizophrenic patients.**/ Le rapport des reves apres administration de reserpine chez des schizophrenes chroniques ayant subi une lobotomie prefrontale. Vie Medicale au Canada Francais (Quebec). 2(9):843-848, 1973.

Dream reports by chronic schizophrenics who have submitted to prefrontal lobotomy after administration of reserpine are presented. An increase in REM phases and provoked awakenings after reserpine administration was reported. Earlier studies suggest that lobotomized schizophrenic patients showed a significantly lower incidence of dream reports in delayed and immediate REM interviews than nonlobotomized patients. Despite the new findings, the incidence of dream recall in lobotomized patients remains significantly lower. Reserpine, which causes a depletion of brain monoamines and impairs the consolidation of memory in animals, does not affect the dream reports in lobotomized or nonlobotomized patients. Results are tabulated and discussed. Possible biochemical and neurophysiological explanations of the results are given. 23 references. (Journal abstract modified)

178224 Kariya, Tetsuhiko; Hirayama, Masami; Shimazu, Yasuo. Department of Neuropsychiatry, Tokyo Medical and Dental University, Japan **Clinical experiences with flupenthixol (FX-703).** Clinical Psychiatry (Tokyo). 13(3):67-78, 1971.

Effects of flupenthixol (FX-703) on schizophrenia were studied in 17 acute and chronic schizophrenics treated orally with FX-703 (increasing dose from 3mg/day to 8mg/day) for 28 to 280 days. The results show; the drug was effective in 3 patients with acute schizophrenia and 7 patients with chronic schizophrenia in improving ego disturbance, delusion, hallucination, physical movement, interpersonal relationships, volition for group activities, and ability in work. These effects appeared within 5 to 6 weeks in most cases. Side-effects, such as sleep disturbance, extrapyramidal syndrome, tachycardia, loss of appetite and constipation disappeared through administration of sleeping pills and antiparkinsonism agents. 12 references.

178255 Gowardman, M.; Barrer, Brigid; Brown, R. A. Kingseat Hospital, Auckland, New Zealand **Pimozide (R6238) in chronic schizophrenia: double blind trial.** New Zealand Medical Journal (Dunedin, New Zealand). 504(78):487-491, 1973.

A double-blind trial of pimozide (R6238), a long-acting antipsychotic drug, is conducted in chronic schizophrenia. The drug is prepared for clinical efficacy by double-blind method with haloperidol in chronic institutionalized and withdrawn schizophrenics, 10 patients in each group. Pimozide was found to have marked ac-

tivating properties in six patients and facilitated socialization of otherwise hopeless or hard core cases. Psychotic symptoms became worse in 4 patients. Extrapyramidal side-effects are considered. Pimozide appears to be a useful addition to the neuroleptic armory in the treatment of some chronic schizophrenics. 13 references. (Author abstract modified)

178545 Reschke, Richard W. County of Los Angeles, Mental Health Services, Long Beach Regional Service, 236 E. Third Street, Long Beach, CA 90812 **Parenteral haloperidol for rapid control of severe, disruptive symptoms of acute schizophrenia.** Diseases of the Nervous System. 35(3):112-115, 1974.

Intramuscular haloperidol, at three dose levels, chlorpromazine, and placebo are compared for efficacy, rapidity of therapeutic onset, and safety in 50 acute psychotic patients requiring rapid control. Global evaluation, BPRS, and target symptom ratings are performed. Results indicate that the 5mg and 2mg haloperidol doses are significantly superior to the 1mg haloperidol and 25mg chlorpromazine doses and to placebo. Transfer of patients to oral haloperidol was satisfactorily accomplished. Side-effects for all medications were minimal and included slight to moderate EPS and drowsiness. The use of antiparkinson drugs completely controlled the extrapyramidal symptoms. 8 references. (Author abstract modified)

178578 Dawson, Susan; Kaplan, Jonathan; Semel, Charles; Green, Richard; Woodrow, Kenneth; Gillin, J. C.; Wyatt, R. J. NIMH, St. Elizabeths Hospital, Washington, DC **Sleep changes in chronic schizophrenics: effects of 5-hydroxytryptophan (5HTP). (Unpublished paper)** Washington, DC, NIMH, 1974. 1 p.

The effect of 5-hydroxytryptophan (5HTP), the immediate precursor of serotonin, on sleep is reported. The sleep of 18 male chroncially hospitalized schizophrenic patients was studied during prolonged 5HTP administration; this was compared to sleep studies of various lengths during the month long placebo periods immediately preceding and following 5HTP administration. Seven of the 18 patients were studied at intermediate doses, 11 at high doses, and 7 during withdrawal from 5HTP. At low dosages of 5HTP there was a significant increase in REM latency, but no other changes in sleep. Total REM and delta sleep were significantly reduced on intermediate dosages and high dosages. Total sleep time and stage 2 were also significantly reduced on high dosages. Patients were agitated and sleep was poor during the first week of withdrawal; however, there was a significant increase in REM percentage and a decrease in REM latency. During the second week of 5HTP withdrawal, all sleep measurements returned to baseline. In addition, at the high dosages, the number of REM periods decreased compared to placebo. Although the length of the first REM period was increased on high 5HTP dosages, the time from onset of the first REM period to the second was unaltered. (Author abstract modified)

180046 Rimon, Ranan. no address **Lithium in the treatment of schizophrenia.** In: Psychiatria Fennica. Helsinki, Helsinki University Central Hospital, 1973. 301 p. (p. 261-263).

Lithium treatment of schizophrenia is discussed. Lithium was found to do little in modifying basic thought disturbance. Other characteristics of schizophrenia generally remained unaltered during therapy. Lithium did work effectively against psychomotor agitation and may be of value during acute schizophrenic episodes in patients with marked affective overlay and/or undulating course of the disease. The prophylactic effect of the drug may be due to a qualitative change in symptomatology. It is felt that the role of lithium in the treatment of schizophrenia requires further elucidation. 23 references.

180153 Bagadia, V. N.; Shastri, P. C.; Sule, S. M.; Shah, L. P. King Edward VII Memorial Hospital, Bombay-12, India **Further experience with fluphenazine enanthate injection.** Indian Journal of Psychiatry (Madurai). 14(3):279-286, 1972.

The effect of fluphenazine enanthate injection was investigated in 118 cases of schizophrenia. Significant improvement occurred in 77% of the patients with poor prognosis. Seventy eight cases were given long-term treatment, up to 6 months. This produced an improvement rate of 84.6%. The drug produced extrapyramidal system side-effects in all but four participants. 6 references. (Author abstract modified)

180154 Jha, B. K.; Bhaskaran, K. Hospital for Mental Diseases, Kanke, Ranchi-6, Bihar, India **Experiences with fluphenazine enanthate in long stay hospitalized schizophrenics.** Indian Journal of Psychiatry (Madurai). 14(3):263-277, 1972.

The effect of fluphenazine enanthate injection was studied in 112 long stay schizophrenic patients. The minimum duration of illness of the patients was 2 years, the maximum 26 years, and the mean 10.4years. Significant improvement occurred in 32.6% of the cases. About 22% were made manageable in the hospital. The most encouraging results were seen in cases of paranoid schizophrenia. Side-effects were seen in 73.2% of cases. Extrapyramidal side-effects and hypotension were commonest. Dystonic reactions were also fairly common and when present were very alarming in nature. There was no correlation between the severity of side-effects and degree of improvement. Fluphenazine enanthate is a useful drug for some chronic schizophrenics resistant to other forms of treatment and it may also be useful for those chronic schizophrenics who show frequent relapses. 41 references. (Author abstract modified)

180319 Nishizono, Masahisa. Dept. of Psychiatry, Kyushu Univ. School of Medicine, Fukuoka, Japan **Psychotropic medication in Japan.** Indonesian Psychiatric Quarterly (Djakarta). 3(3/4):58-64, 1970.

The development of psychotropic medication in Japan, with special attention to the treatment of schizophrenia, is discussed. Modern psychiatric services in Japan started with lectures in psychiatry at Tokyo Medical College in 1901. In 1952, chlorpromazine and reserpine were introduced to psychiatric treatment. The psychiatric service of Japan focuses attention on the psychotropic medication for schizophrenia. The remission cases are rather stable at 60%, from the period when only chlorpromazine and reserpine were available. Drugs of choice in various types of schizophrenia are summarized. Drugs are effective in removing positive symptoms such as hallucination, delusion, and excitement. Negative symptoms accompanied by very little psychic tension and assaultive symptoms are not readily removed despite the use of all kinds of drugs. The appearance of psychotropic drugs has markedly reduced the use of insulin shock therapy and electroconvulsive treatment. The psychiatrists in Japan have begun to guard themselves against the danger of overdependence on drugs.

180675 Glatzel, J. Neuro-Psychiatrischen Klinik der Johannes-Gutenberg Universitat, Mainz, Germany **/Experience gained in the treatment of chronic schizophrenic psychoses with a thioridazine derivative./** Erfahrungen bei Behandlung chronisch schizophrener Psychosen mit einem Thioridazinderivat. Medizinische Welt (Stuttgart). 23(2):62-64, 1972.

The results of treating 50 female patients suffering from chronic szhizophrenia or involutional psychosis with Inofal, a side chain, sulfone or thioridazine, are discussed. Inofal proved effective in the treatment of productive psychotic symptoms, particularly for acute delusional hallucinatory manifestations in chronic schizophrenics. The psychosis was reduced in most cases within a short period of time to interval symptoms. Average treatment lasted 10 weeks. The drug was administered orally, 150 to 250mg/day, increased in individual cases up to 600mg/day. A therapeutic effect usually was observed within 6 to 8 days. Results of treatment of involutional psychoses were negative. Side-effects were minor, with the heavily sedative effect the only one of significance. Circulatory effects were minor. The observation that those recidivistic psychoses which constitute a special clinical problem, particularly in large mental hospitals, respond rapidly to treatment with Inofal, and reliably is of great practical significance. 12 references.

181153 Howard, James S., III; Schmidt, Kurt T. Eastern State Hospital, Williamsburg, VA **End of a back ward: the rapid rehabilitation and release of chronically hospitalized psychiatric patients.** Psychosomatics. 14(6):355-361, 1973.

An intensive program in a state mental institution to get chronic, long-term mental patients (71% diagnosed as schizophrenic) back into the outside world is described. Although it required no staff increase or use of extra resources, the program was successful in recombining and reorganizing different aspects of the treatment program to enable patients to improve enough to be released. These aspects include the milieu, occupational therapy, group therapy and chemotherapy, with emphasis on the latter. 8 references.

181192 Marriott, Peter, F.; Grigor, John, M. G.; Hiep, Albert; Znaniecka, Vicki. Royal Park Psychiatric Hospital, Royal Park, Vic. 3052, Australia **A psychiatric clinic for depot phenothiazines.** Medical Journal of Australia (Sydney). 2(21):957-960, 1973.

A clinic established in an acute psychiatric hospital to administer fluphenazine decanoate to

outpatient schizophrenics is described. The pharmacology of fluphenazine decanoate is discussed, and the Modecate program and clinic are presented. In addition to the administering of medication, needs such as assistance with accomodation and employment, and supportive psychotherapy for the patient and family are offered. In time the patient usually establishes a warm relationship with the treatment team and attends more regularly without prompting. It is noted that the clinic growth in 1972 was in excess of 300%. 18 references.

181378 Amakusa, Tairiku; Majima, Takejiro. Department of Psychiatry, Juntendo University, Japan **The comparison of therapeutic effects of FK-880 (sulpiride) and perphenazine in schizophrenia by a double-blind controlled study.** Juntendo Medical Journal (Tokyo). 19(2):239-249, 1973.

The effects of sulpiride on schizophrenia were compared with perphenazine in a double-blind controlled study. After 6 weeks, statistics showed that there was no significant difference in the therapeutic effects between the groups. But in patients suffering from schizophrenia for over 5 years, sulpiride showed more positive effects than perphenazine. Perphenazine was more effective in improving hallucination than sulpiride. In the incidence of side-effects, no significant difference was observed between the groups. 17 references. (Journal abstract modified).

181778 Bazhin, E. F.; Rafalovich, E. G. Leningrad Psychoneurological Institute, Psychiatric Ward No. 2, Leningrad, USSR /**Treatment of hallucinatory disorders in schizophrenia by atropine comas.**/ Lecheniye gallyutsinatornykh rasstroystv pri schizofrenii atropinovymi komami. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 73(8):1223-1227, 1973.

Treatment of hallucinatory disorders in schizophrenia by induced atropine comas is described. A total of 52 schizophrenic patients were treated. A disappearance or reduction of hallucinatory symptoms was reported in 30% of the cases. Following the course of atropine comas the patients exhibited increased sensitivity to neuroleptics. The use of haloperidol had good results in 45% of the patients treated. 18 references. (Journal abstract modified)

09 DRUG TRIALS IN AFFECTIVE DISORDERS

174995 Rosenblatt, Seymour; Chanley, Jacob D. Department of Psychiatry, Mount Sinai School of Medicine, Basic Sciences Bldg., 10 E 102nd St., New York, NY 10029 **Measuring the pharmacological action of imipramine in the treatment of depressions.** Archives of General Psychiatry. 30(4):456-460, 1974.

The pharmacological action of imipramine in the treatment of depression was studied. The pharmacological action of imipramine hydrochloride was determined by a method involving the infusion of tritiated norepinephrine and measuring the tritiated metabolites in urine. The effects of similar dosages of imipramine on norepinephrine metabolism varied between subjects and were probably due to individual differences in drug metabolism. A significant correlation was found between an index of the reuptake inhibition by imipramine on peripheral sympathetic nerve endings and the improvement in the clinical state of depressed patients. 29 references. (Author abstract modified)

175069 Hirata, Junichiro. Okayama University, Okayama, Japan **Electroencephalogram of hysteric patients.** Clinical Electroencephalography (Osaka). 13(6):392-401, 1971.

Treatment of hysterical patients exhibiting spasmodic abnormal electroencephalograms is discussed. A sample of male and female patients ranging in age from 2 to 17 years and including those suffering from hysteria only, and those with complications was covered. Symptoms were physical (paralysis, cramps), sensory (numbness), perceptual - emotional (dementia, slow reflexes) and neurological (heavy breathing). Hysteria, impassivity and introversion were characteristic signs. Treatment should include therapy and consultation in addition to medical attempts. Drugs such as diphenylhydantoin, phenobarbital and other epilepsy controlling drugs were, in general, ineffective. Antianxiety drugs such as diazepam and chlordiazepoxide were effective in four out of nine cases. Levomepromazin was most effective. After 9 years of research it was discovered that 60% of hysterical patients had organic deficiencies, but long-term research is needed to improve treatment techniques. 26 references.

175120 Ohsawa, Ikuko; Ohuchida, Shoji. Department of Neuropsychiatry, Japanese Red Cross

Medical Center, Japan **A case of Werner's syndrome with schizophrenia-like symptoms.** Clinical Psychiatry (Tokyo). 15(3):257-266, 1973.

The development of a case of Werner's syndrome with schizophrenia like symptoms is examined. Convulsions appeared on a yearly basis after having measles at 3 years old. A type of catatonia occurred at 14 years. EEG abnormality did not appear until 20 years of age, when the frequency of convulsions increased. Chlordiazepoide has been used since the patients' twentieth year. Gross physiological symptoms (hair loss and skin disorder) and severe schizophrenic symptons are controlled presently with special diet and 150mg/day of chlordiazepoxide. 33 references.

175410 Nandi, D. N.; Ajmani, Savita. R. G. Kar Medical College, Calcutta, India **A trial of trimipramine.** Indian Journal of Psychiatry (Madurai). 14(2):223-226, 1972.

Relative potency of a drug of the trimipramine group in treatment of depressive cases used in conjunction with sleeping pills (promethazine and amylobarbitone) and chlordiazepoxide vs. placebo was assessed. A significant improvement in cases of symptoms of self-reproach or guilt, anxiety, social withdrawal, and others was shown. It is concluded that trimipramine has better therapeutic value for the treatment of endogenous depression than a placebo. 5 references. (Author abstract modified)

175583 no author. no address **General practitioner clinical trials. A long-acting amitriptyline preparation.** Practitioner (London). 209(1253):700-705, 1972.

A trial of a new long acting amitriptyline preparation is discussed. The trial was confined to patients with depression who were already being treated with amitriptyline, since the object of this trial was to determine whether S-R amitriptyline is an effective form of maintenance therapy. Dosages and further clinical data are discussed. Results are assessed initially, and at the end of each 3-week treatment period, using standardized assessments of global severity and the General Practitioner Research Group neurotic depression 8-item rating scale. Topics considered include global assessments, symptom ratings in detail, and side effects. Similar effects were evident from the sustained - release amitriptyline preparation (lentizol) given in a single night-time dosage of 50-100 mg.,as compared with the standard preparation given in a dosage of 25 to 50 mg. thrice daily. There was also less drowsiness with the long acting preparation. The advantages of a sustained - release (S-R) capsule of amitriptyline hydrochloride (lentizol) are presented, being a single dosage at night with the equivalent dosage being less than that required in thrice daily medication.

176475 Yamaguchi, Nariyoshi; Kuratomo, Masayoshi. Kanazawa University Medical School, Japan **Experience in the use of an antidepressive, clomipramine (anafranil), in psychiatric out-patients.** Medical Consultation and New Remedies (Tokyo). 8(5):171-180, 1971.

The effects of clomipramine on depression was studied, based on an experiment in which 25 patients, primarily manic-depressives, were treated with this drug (10 to 60mg/day) for 4 to 280 days. The drug had a strong therapeutic effect in more than half. Clomipramine was also very effective on insomnia when given before bedtime and facilitated longer and deeper sleep. Minor side-effects were observed at the beginning of treatment in 13 patients, such as constipation, fatigue, decrease of blood pressure, vomiting and loss of appetite. 8 references.

176565 Murazaki, Mitsukuni; Taneda, Masao; Oguchi, Toru; Sato, Kiichiro; Mochizuki, Yasunori. Department of Neuropsychiatry, Kitazato University School of Medicine, Japan **Clinical experiences with an antidepressive drug, Noritren (nortriptyline).** Medical Consultation and New Remedies (Tokyo). 9(10):2197-2207, 1972.

Results of the use of Noritren, an antidepressive manufactured in Denmark, as administered to patients with various types of depression by the Department of Neuropsychiatry, Kitazato University, are discussed and tabulated as they compare to results with other drugs. The chemical composition of Noritren, or Nortriptyline as it is more commonly know, is such that as a monomethyl ampitriptyline derivative, it acts in the living organism as an active metabolite. Results are tabulated by age and sex, diagnosis, primary symptoms, number of days of use of drug, maximum daily dosage, use in combination with other drugs, accompanying symptoms, results, and duration of effectiveness. The drug was found to be very effective in 62.3% of all cases. Symptoms virtually disappeared, and patients were able to live a normal social life. Effectiveness was 100% among patients whose primary symptom was depression,

and among those with masked depression. 19 references.

176889 Taen, Shuji; Okada, Michio; Uchimura, Yukio; Takemura, Norio; Sugimura, Noriyuki. Department of Psychiatry, Kanto Teishin Hospital, Tokyo, Japan **Anti-depressant effects of d-chlorpheniramine -- clinical evaluation (first report).** Clinical Psychiatry (Tokyo). 13(11):23-30, 1971.

The effect of d-chlorpheniramine on depression was studied, based on an experiment in which 71 patients with depression were treated with this drug (12 to 30mg/day orally or 18 to 34mg/day, i.v.)with or without other drugs, such as nitrazepam, brovarin, isomytal, chlordiazepoxide, diazepam, chlorpromazine. The results show: this drug was effective in 66% of the patients. Patients with endogenous depression showed extreme and moderate improvement in 72% of the cases. Side-effects, such as drowsiness, delusion and insomnia, occurred in 26% of the Ss. These side-effects immediately disappeared after termination of treatment with this drug. 17 references.

177567 Takahashi, Ryo; Sato, Yorio; Ito, Hitoshi; Kawakita, Yukio; Kudo, Yoshio; Kurihara, Masanao; Tanimukai, Hiroshi. no address **A double blind controlled study comparing protriptyline and amitriptyline.** Clinical Psychiatry (Tokyo). 13(6):635-645, 1971.

The effect of protriptyline (Pr) on depression is compared to that of amitriptyline (Am), based on a double-blind test in which 35 Ss with endogenous depression were treated with Pr and 32 with Am. Pr was effective in 62.9% and Am in 65.6% of the patients, indicating no significant difference in effect between the two drugs. The two drugs were equally effective on various symptoms, but Am was more effective than Pr on sleep disturbance, anxiety and dry mouth. Prior to the treatment, physical symptoms, such as loss of appetite, fatigue, and dry mouth were observed in 50 to 70% of the patients, and drowsiness, dizziness, perspiration, in 20%. Aggravation of these physical symptoms was observed in less than 10% of the patients 3 weeks after treatment. Pr induced abnormal urine protein level in two patients and hepatic disturbance in one; Am induced hepatic disturbance in two. 21 references.

178113 Doig, Marion T., III.; Heyl, Michael G.; Martin, Dean F. University of South Florida, Tampa, FL 33603 **Lithium and mental health.** Journal of Chemical Education. 50:343-345, 1973.

The use of lithium in the treatment of mental patients with manic depressive disorders is discussed. The history of its use is traced and several case histories are briefly noted. Possible mechanisms of action are discussed through references to the literature and therapy experience. 17 references.

178114 Schildkraut, Joseph J. Harvard Medical School, Boston, MA **Neuropharmacological studies of mood disorders.** In: Zubin, J., Disorders of Mood. Baltimore, Johns Hopkins Press, 1972. (p. 65-84).

The possible role of norepinephrine in disorders of mood was studied. Data are presented indicating the effects of imipramine and other tricyclic antidepressants on the turnover and metabolism of norepinephrine in the rat brain. Emphasis is given to the recent finding that the effects of acute and chronic administration of imipramine on norepinephrine turnover are different. It is concluded that these differences may help explain the need for chronic administration of tricyclic compounds in order to cause clincal antidepressant effects. Findings from clincal studies of norepinephrine metabolism in patients with affective disorders are summarized. 45 references.

178432 Gillin, J. C.; Van Kammen, D. P.; Murphy, D. L.; Graves, J.; Wyatt, R. W. A. White Bldg., Rm. 536, St. Elizabeths Hospital, Washington, DC **Differential effects of d- and l-amphetamine on the sleep of depressed psychiatric patients on and off lithium carbonate treatment. (Unpublished paper).** Washington, DC, NIMH, 1974. 1 p.

The effects of d-amphetamine and l-amphetamine on human sleep were compared both before and during treatment with lithium carbonate. Some evidence suggests that the two isomers have equal blocking effects on dopamine reuptake whereas d-amphetamine preferentially blocks norepinephrine reuptake as compared with l-amphetamine. Lithium carbonate, on the other hand, has been reported to enhance norepinephrine reuptake. The data from four moderately depressed psychiatric inpatients (3 female, 1 male; age 30-57) was analyzed. The data indicate that both d-amphetamine, and l-amphetamine suppressed total sleep TS time and sleep efficiency SE. Lithium carbonate did not alter the effects of d-amphetamine and l-amphetamine. Little or no immediate REM rebound was observed following amphetamine administration. (Author abstract modified)

178623 Matsumoto, Kei; Matsushita, Kensuke; Kamizaki, Yasushi; Yoshida, Shuzo; Hatanaka, Hiroyuki; Kawaike, Koji. Dept. of Neuropsychiatry, Faculty of Medicine, Kagoshima University, Japan **Studies on the urinary excretion of catecholamines and 17-ketosteroid in manic-depressive psychosis.** Clinical Psychiatry (Tokyo). 13(9):73-80, 1971.

Urinary excretion of catecholamines and 17-ketosteroid (17-KS) and its relation to symptoms of manic-depression was studied. The effect of chlorpromazine on the excretion of these metabolites was also examined. 17-KS excretion seemed little related to presenting symptomatology. The level of noradrenaline excreted does seem dependent on clinical state and is modified by chlorpromazine. 25 references.

180297 Kline, Nathan S. Research Center, Rockland State Hospital, Orangeburg, NY 10962 **Antidepressant drugs.** Indonesian Psychiatric Quarterly (Djakarta). 5(1):86-99, 1972.

A discussion is presented of the use of antidepressant drugs. Treatment of depression alone or in combination includes: psychotherapy, electroconvulsive therapy, and pharmacotherapy. The two major drug groups are the tricyclics including related drugs such as doxepin and the monoamine oxidase inhibitors. In addition, the thiothixenes in schizoaffective disorders and the phenothiazines should be considered. Lithium constitutes a special case since its primary function in depression is prophylaxis against recurrence. The tricyclics and related drugs for the treatment of depression, listed in descending order of sedative and antianxiety properties, include: doxepin (Sinequan), amitriptyline (Elavil), nortriptyline (Aventyl), imipramine (Tofranil), desipramine (Pertofrane, Norpramin), and protriptylin (Vivactil). The medical conditions requiring caution in the use of tricyclics and common side-effects are summarized. The monoamine oxidase inhibitors for the treatment of depression include: isocarboxazid (Marplan), nialamide (Niamid), phenelzine (Nardil), and tranylcypromine (Parnate). The medical conditions in which MAO inhibitors should be used cautiously are discussed.

180406 Gajwani, A. K.; Sharma, Shridhar. Department of Psychiatry, Goa Medical College, Panaji-Goa, India **Diagnosis and management of depression in general practice.** Clinician (Goa). 37(4):140-144, 1973.

Three criteria for diagnosis of depression are examined, classifications of diagnosis with precipitating causes are discussed, and management procedures are reviewed. The characteristics of psychotic depression and neurotic depression are compared. Drugs used in the treatment of depression are listed with indicated dosages and side-effects. 8 references.

181158 Ford, R. Bruce; Beyer, Emanuel C. 943 N. Church St., Spartanburg, SC 29303 **Tic de Gilles de la Tourette: case report and brief discussion.** Journal of the South Carolina Medical Association. 70(1):1-3, 1974.

A case report and brief discussion of Tic de Gilles de la Tourette's disease is given. Previous methods of treatment are presented, such as electroshock, behavior modification, psychotherapy, and major tranquilizers, with haloperidol proving to be the most effective control of the disease. Etiology, observations and symptoms are discussed. 13 references.

181274 Ablon, Steven L.; Goodwin, Frederick K. Children's Center, McLean Hospital, Belmont, MA **High frequency of dysphoric reactions to tetrahydrocannabinol among depressed patients.** American Journal of Psychiatry. 131(4):448-452, 1974.

A scale for dysphoria reactions is correlated, as well as personality variables derived from clinical observations and MMPI. A controlled systematic study of the effects of THC on a homogeneous population of depressed patients was conducted. The hypothesis that dysphoric reactions to THC are more common among patients with unipolar than bipolar affective illness is examined. A double-blind design test was used on 13 hospitalized depressed patients at NIMH. Four of the patients' case histories are examined in detail. These data suggest that patients with unipolar depressive illness represent a high-risk group for the occurrence of dysphoric reactions to moderate amounts of THC. THC could most accurately be described as a mood intensifier rather than as a euphoriant per se. Personality characteristics and responses to THC are tabulated for each patient by age.

181358 Goodwin, Frederick K.; Sack, Robert L. Laboratory of Clinical Science, NIMH, Bethesda, MD 20014 **Central dopamine function in affective illness: evidence from precursors, enzyme inhibitors and studies of central dopamine turnover. (Unpublished paper).** Bethesda, MD, NIMH, 1973, 47 p.

The role of central dopamine function in affective illness is discussed. The data reviewed focus on clinical/biochemical correlations obtained from manic depressive patients undergoing treatment with three experimental drugs (L-DOPA, AMPT, and fusaric acid) which affect brain catecholamine synthesis. It is suggested that differences in the behavioral response to experimental drugs which alter brain catecholamines, particulary brain dopamine, are determined not only by the biochemical effects of the drug but also by psychobiological differences between subgroups. In relation to the hypothesized role of central amines in schizophrenia as well as in affective illness, it is suggested that a disturbance in a given central amine system may not correlate as well with a specific diagnosis as it might with specific symptom profiles which themselves overlap diagnostic categories. 65 references.

10 DRUG TRIALS IN NEUROSES

175286 Zung, William W. K. Duke University Medical Center, Durham, NC 27705 **The differentiation of anxiety and depressive disorders: a psychopharmacological approach.** Psychosomatics. 14(6):362-366, 1973.

Clorazepate dipotassium (CAP) was examined for its antianxiety and antidepressant properties, considering whether such drugs should be redefined. A total of 275 patients exhibiting anxiety were studied, none exhibiting organic or psychotic symptoms. Both single and double-blind techniques were employed, with anxiety measured by the Hamilton Anxiety Scale, the Zung Self-rating Anxiety Scale or the Zung Self-rating Depression Scale. CAP given as a single bedtime dose clearly relieved symptoms of anxiety and depression as measured on the two Zung scales. This duality may be explained by the limbic system which is charged with the close integration of many disparate brain functions into one orderly whole, with consequent inability to localize and control disturbances in its many subsystems. Additional studies are required to elucidate mixed anxiety and depressive states. 14 references.

175967 Bagadia, V. N.; Dave, K. P.; Karnik, N. R.; Pradhan, P. V.; Shah, L. P. Department of Psychiatry, K. E. M. Hospital, Parel, Bombay 12, India **Trioxazine in the treatment of neurosis.** Indian Journal of Psychiatry (Madurai). 15(2):187-192, 1973.

An open uncontrolled study of Trioxazine as a treatment for anxiety and tension states is reported. The drug was administered to 100 patients with neuroses, and 22% of patients with anxiety neurosis, 12% of patients with chronic anxiety neurosis, and 25% of patients with depression, phobia, or hysteria showed significant improvement. Side-effects and followup treatment are discussed. 3 references.

176107 Rickels, Karl; Schneider, Benjamin; Pereira-Ogan, Jorge A.; Perloff, Milton M.; Segal, Asher; Vandervort, William. University of Pennsylvania, Philadelphia, PA **Pipradrol in mild depression: a controlled study.** Journal of Clinical Pharmacology. 14(2-3):127-133, 1974.

A double-blind placebo controlled trial of pipradrol (5.0to 7.5mg per day) was conducted with 111 mildly to moderately depressed patients treated in nonpsychiatric practice. Only a few patient but no physician measures indicated any superiority for pipradrol over placebo in the 80 patients who completed the study, and this occurred only in those patients who were initially more depressed. Pipradrol caused significantly more side-effects, particularly stimulatory and autonomic effects, and was associated with significantly more anorexic effects and weight loss than placebo. Present results thus suggest at the most only limited efficacy for pipradrol in the treatment of depressed outpatients. 9 references. (Author abstract)

176286 Haider, Ijaz. Government Mental Hospital, Lahore, Pakistan **Lorazepam in the treatment of anxiety.** Journal of the Pakistan Medical Association (Karachi). 23(3):77-80, 1973.

A double-blind study was carried out in 50 patients suffering from anxiety by using lorazepam, a new benzodiazepine, and diazepam. The drugs appeared to be equally effective in all respects, and no drug induced changes were noted from urine examination or blood pressure recordings. 6 references. (Author abstract modified)

176448 Kimura, Yoshihide; Midorikawa, Yoko. Okaya Hospital, Japan **Experience in the use of imipramin.** Medical Consultation and New Remedies (Tokyo). 8(10):205-208, 1971.

The effect of imipramine on depressive states in the field of obstetrics and gynecology is studied. Thirty 23- to 74-year-old female patients with depression, insomnia, anxiety,

etc.,accompanied with various obstetrical and gynecological disturbances, were orally treated with this drug (10 to 20mg/day) for 3 days to 1 month. Imipramine was effective in 70% of the patients and effective on insomnia, anxiety, irritation, stiff shoulder, pain in the intestine, nausea, and dizziness. No side-effect was observed. 3 references.

176473 Okuse, Satoshi; Saito, Nobuo; Shigeyoshi, Takahashi; Ishibashi, Fumitoshi; Takasu, Shigeya; Wada, Takeo. First Department of Internal Medicine, Sapporo Medical College, Japan **Clinical pharmacological study of bromazepam in the field of internal medicine.** Journal of Japanese Psychosomatic Society (Tokyo). 11(5):329-339, 1971.

The effect of bromazepam on psychosomatic diseases was studied in a double-blind cross-over test in which 37 patients with various psychosomatic diseases were treated with this drug (15mg/day) for 14 days preceded or followed by placebo (15mg/day) for 14 days. The results show that among 30 patients who completed the test, 17 patients showed moderate or remarkable improvement of depression, insomnia and muscle tension. Among the 37 patients, 22 had side-effects, such as sleepiness, muscle relaxation, disturbance in gait, excitation and anxiety, and 7 of these dropped out of the test. Although the side-effects diminished rapidly by decreasing the dose in some cases, the dose of 15mg/day is excessive for habitual use in the field of internal medicine. A further study is necessary to determine the appropriate daily dosage. 6 references. (Author abstract modified)

176474 Tsukamoto, Ryuzo; Etsuraku, Masayo; Ono, Masahiro. Asahikawa Hospital, Japan **Experience in the use of Sinequan (doxepin hydrochloride).** Medical Consultation and New Remedies (Tokyo). 8(10):193-197, 1971.

The effect of Sinequan (doxepin hydrochloride) on depression was studied in 15 17- to 61-year-old patients, primarily neurotics, treated with this drug (40 to 225mg/day) for 14 to 54 days, with or without treatment with other drugs. Sinequan was therapeutically effective in 11 patients. This drug had a moderate effect on depression and lack of volition and was noneffective on hypochondriac tendency. The most successful dosage appeared to be 75mg/day. Minor side-effects, such as dry mouth, were observed but were minimal. 6 references.

177376 Rickels, Karl; Downing, Robert W. 203 Piersol Bldg., University Hospital, 3600 Spruce St., Philadelphia, PA 19104 **Predicting relief from anxiety with phenobarbital.** Psychosomatics. 15(1):30-34, 1974.

Use of phenobarbital in treating anxiety is discussed. A double-blind placebo controlled drug study was made on anxious, neurotic outpatients in an attempt to define the nonpharmacological characteristics associated with a favorable treatment response to the medication. Thirty two potential predictors of improvement were chosen and the variables included: demographic characteristics; patient attitudes and expectations; physician attitudes and expectations; and illness characteristics. Global improvement was used as the dependent variable. Predictors of good treatment response irrespective of treatment agent prescribed were income of head of household, marital status, prognosis and initial level on the patient Symptom Checklist Performance Difficulty Factor. Independent of the selected predictors, phenobarbital alone produced significantly more improvement than placebo in the anxious population. 18 references. (Author abstract modified).

178038 Prasadio, Triman. Department of Neurology and Psychiatry, University of Airlangga, Surabaya, Indonesia **/Tacitin treatment for the patient with anxiety./** Pengobatan Tacitin pada penderita dengan kecemasan. Indonesian Psychiatric Quarterly (Djakarta). 6(2):103-109, 1973.

Use of tacitin in the Dr. Sutomo Hospital is discussed. The decision was made to test it in December, 1971, on patients in the polyclinic suffering from tension, anxiety, and minor depression. Forty seven patients were given dosages ranging from 15 to 90mg daily over a period of 4 weeks. Results are tabulated: 61.7% showed excellent improvement; 23.4% showed moderate improvement; 10.6% showed slight improvement; and 4.3% evidenced no improvement. There were no significant side-effects. Test results indicate that Tacitin is effective in the treatment of anxiety cases, and that its tolerability is outstanding. 13 references.

178544 Kiev, Ari. no address **The role of chemotherapy in managing potentially suicidal patients.** Diseases of the Nervous System. 35(3):108-111, 1974.

Experience gained at the crisis intervention clinic of the Cornell Program in Social Psychiatry

is summarized to demonstrate the value of chemotherapy as part of an overall approach to treating potentially suicidal patients. A double-blind study shows that doxepin is therapeutically comparable to amitriptyline and that both drugs are significantly better than placebo in the treatment of neurotic depression among adult outpatients attending the clinic. 8 references. (Author abstract modified)

178811 Rodrigues, V. R. Rua Miguel Bombarda, 830 Ermesinde, Portugal **Effect of a carnitine-cyproheptadine combination on anorexia and weight gain in children.** Panminerva Medica (Torino). 15(7-8): 259-261, 1973.

The effect of a carnitine - cyproheptadine combination on anorexia and weight gain in children was examined. In a clinical trial with a combination of DL-carnitine - cyproheptadine, a very potent stimulation of appetite and weight gain indicates that this combination is a good preparation for the treatment of anorexic children. The carnitine acts by improving intestinal absorption, while cyproheptadine acts more centrally. No side-effects were observed. 13 references. (Journal abstract modified)

180048 Trappe, B. Haaga Rehabilitation Institute, Central Mental Hospital, Helsinki, Finland **Doxepin and amitriptyline-chlordiazepoxide-combination in neurotic states: a comparative double blind study.** In: Psychiatria Fennica. Helsinki, Helsinki University Central Hospital, 1973. 301 p. (p. 269-275).

The effects of doxepin and amitriptyline chlordiazepoxide were examined in neurotic patients with anxiety and depression. Results indicate that psychic status, depression, and anxiety improved more with doxepin than with amitriptyline chlordiazepoxide. On somatic symptoms the favorable effects of both drugs were almost equal. Side-effects were slight and easily controllable. 13 references.

180062 Tesarova, O. Institute for Postgraduate Medical and Pharmaceutical Studies, Bratislava, Czechoslovakia **Experimental depression caused by apomorphine and phenoharmane.** Pharmakopsychiatrie Neuropsychopharmakologie (Stuttgart). 5(1):13-19, 1972.

Apomorphine and phenoharmane administration in neurotics and the mentally healthy was studied to determine the effects on depression. The generation of depression or dysphoria by apomorphine and phenoharmane is proof of the depressiogenic effect of both compounds. The direct dependency between the aroused depression and the effect of drugs may explain the selectivity of the depressiogenic effect of both materials. These results might contribute to the field of study involving the etiopathogenesis of endogenous depressions. 17 references.

180064 Akpinar, S.; Itil, T.; Rudman, S.; Hsu, W.; Sletten, I. Missouri Institute of Psychiatry, 5400 Arsenal Street, St. Louis, MO 63139 **Comparison of the clinical and computer analyzed EEG effects of mesoridazine and chlorpromazine.** Pharmakopsychiatrie Neuropsychopharmakologie (Stuttgart). 5(1):25-34, 1972.

The EEG effects of mesoridazine as compared to those of chlorpromazine were investigated. Mesoridazine produces significant improvement in the period while chlorpromazine produces improvement in less than half the time. In terms of BPRS ratings, the differences between the two drug groups are not significant in any time period. Mesoridazine produces an increase of slow and fast waves in the EEG which is characteristic of antidepressive drugs. Clinical and EEG findings confirm that mesoridazine has antidepressive properties, in addition to an antipsychotic effect. 18 references. (Author abstract modified)

180146 Haider, Ijaz. Welsh National School of Medicine, Whitchurch Hospital, Cardiff CF 4, England **WY-4036 (lorazepam) -- a new tranquilizer.** Pakistan Medical Forum (Karachi). 6(9):27-32, 1971.

The effect of WY-4036 (lorazepam) was studied in 50 patients (30 females and 20 males) all suffering from a neurotic anxiety illness or anxiety associated with depression in a double-blind controlled trial. The treatment lasted for 3 weeks. Patients were assessed before the start of the trial and at intervals of 1, 2, and 3 weeks. At the fourth and final assessment, a four point global assessment was also made and expressed as greatly improved, improved, no change, or worse. The overall distribution of total scores at the pretrial assessment are similar for WY-4036 and placebo, but the mean score was better on WY-4036 than on placebo for each week. The global assessment also shows that WY-4036 is significantly better as a tranquilizer than placebo. 1 reference. (Author abstract modified)

180249 Katira, M. N.; Iyer, D. S. Lokmanya Tilak Municipal General Hospital, Sion Bombay, India **A double blind trial of trioxazine with placebo in anxiety states.** Indian Journal of Psychiatry (Madurai). 14(3):287-288, 1972.

A double-blind trial of Trioxazine and placebo was carried out on 50 outpatients attending the psychiatric department of Lokmanya Tilak Municipal General Hospital, Sion. There was no difference in the effect of placebo and Trioxazine in anxiety neurosis. The dropout rate was a very high, 52%. 6 references. (Author abstract modified)

180986 Goto, Akio; Kajiyama, Susumu; Noguchi, Takuro; Murabayashi, Rihei; Murakami, Toshio; Haneba, Norihito; Okuma, Fumio; Harada, Toshio. Tokyo Metropolitan Matsuzawa Hospital, Japan **Double-blind comparative study of HF-1972/noveril in depression.** Medical Consultation and New Remedies (Tokyo). 9(9):1965-1976, 1972.

The results of the administration of Noveril and Amitriptylene in depression once a day for 8 weeks are reported and tabulated by age, sex, illness, past frequency cycle, past length of cycle, condition before and after medication, and the effects obtained from the two drugs. Summaries reveal a slight improvement in 88% of patients on Noveril and the same degree of improvement in 84% of those on Amitriptylene. Patients showed more improvement with respect to depression, speaking and thinking after the fourth week on Noveril. From the fourth to eight weeks of the tests, the daily behavior of those on Noveril was better than that of those on Amitriptylene. Side-effects appeared similar for both drugs.

181072 Gottschalk, Louis A.; Stone, Walter N.; Gleser, Goldine C. Dept. of Psychiatry and Human Behavior College of Medicine, University of California, Irvine, CA 92664 **Peripheral versus central mechanisms accounting for antianxiety effects of propranolol.** Psychosomatic Medicine. 36(1):47-56, 1974.

A beta-adrenergic blocking agent, propranolol (6-mg orally in three divided doses over a 12 hr period), significantly reduced basal anxiety scores in 12 similar subjects. In response to a 10 min stress interview, anxiety scores increased to equal levels, whether subjects were on propranolol or a placebo. On placebo, anxiety scores correlated positively with average plasma FFA. On propranolol, anxiety scored correlated negatively with plasma FFA and the average pulse rate was significantly lowered. The experimental findings suggest that basal or resting anxiety may be maintained by peripheral afferent autonomic biofeedback, and the latter can be reduced by beta-adrenergic blocking agents; whereas the magnitude of acutely aroused anxiety is mediated more through the central nervous system. 32 references. (Author abstract)

181273 Rickels, Karl; Downing, Robert W. Dept. of Psychiatry, Univ. of Pennsylvania, 203 Piersol Bldg., University Hospital, 3400 Spruce St., Philadelphia, PA 19104 **Chlordiazepoxide and hostility in anxious outpatients.** American Journal of Psychiatry. 131(4):442-444, 1974.

Several analyses to examine the effects of chlordiazepoxide on anxiety, hostility and irritability were conducted. Most of the 120 outpatients who were placed on the drug were married White women, with a mean age of 42. A second group of 105 subjects on placebo during the three clinical trials were also seen in three different treatment settings. It was concluded that chlordiazepoxide proved significantly better than placebo in reducing hostile, irritable, and anxious symptomatology in 225 anxious neurotic outpatients. The findings reported here failed to confirm previously observed increases in hostility, believed to be induced by chlordiazepoxide. It is felt that there is little justification for avoiding use of chlordiazepoxide by anxious outpatients with concomitant hostility and irritability. Further research is also suggested. 9 references. (Journal abstract modified)

181957 Sakalis, G.; Oh, D.; Gershon, S.; Shopsin, B. Neuropsychopharmacology Research Unit, Department of Psychiatry, New York University Medical Center, 550 First Ave., New York, NY 10016 **A trial of Gerovital H-3 in depression during senility.** Current Therapeutic Research. 16(1):59-63, 1974.

Ten senile - arteriosclerotic patients with features of depression were given Gerovital H-3 (100 to 200mg) i.m. three times per week for 3 weeks. The majority of cases required the maximal dose; no side-effects were recorded. The drug was found to have a mild euphoriant effect which, however, was partly obscured by the variability in the clinical picture of dementia. It is considered that the most likely mechanism by which the drug brings about its effect is a reversible inhibition of

monoamine oxidase, the levels of which have recently been found to increase with age. 9 references. (Author abstract)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

175047 Skopkova, H. Psychiatricka lecebna, Dobrany, Czechoslovakia **/Psychotic complications after tetraethylthiuramdisulfide used in the treatment of alcoholism./** Psychoticke komplikace tetraetylthiuramdisulfidu pouzivaneho v protialkoholni lecbe. Ceskoslovenska Psychiatrie (Praha). 69(2):103-111, 1973.

Therapeutic effects and complications of antabuse - tetraethythiuramdisulfide treatment of chronic alcoholics are described. The hypothetic origin of disulfiramid psychoses and several opinions about its etiology in literature are reviewed. Twenty nine cases of antabuse psychoses in a study dealing with 1348 patients during alcoholic treatment are described. The average psychotic period was 21 days and usually occurred after 35 days of antabuse dispensation. These periods were characterized by the following: disorders of mood aggressivity, delirious states, bizarre delusions, illogical speaking, and disorders of thinking. The performed antabuse alcohol reaction phenomenon was directly related to the psychoses in over half the cases studied. The possible prevention of antabuse psychoses was also discussed. 15 references. (Author abstract modified)

175393 Bagadia, V. N.; Kotwani, P. N.; Dave, K. P.; Saraf, K. R.; Shah, L. P. Psychiatric Department, K.E.M. Hospital, Bombay 12, India **Flupenthixol in certain psychiatric illnesses.** Indian Journal of Psychiatry (Madurai). 14(1):19-23, 1972.

A clinical trial to study the effect of Flupenthixol, a new Thioxanthine derivative, in patients suffering from anxiety states, depression, behavior problems associated with epilepsy and other organic states, and symptoms of delirium tremens in chronic alcoholics is reported. Delirium tremens was controlled, and significant improvement was seen in 30% of the patients with anxiety states, 33% with depression, and 66% with behavior problems. Results and side-effects are discussed. 9 references. (Author abstract modified)

175426 Loranger, Armand W.; Goodell, Helen; McDowell, Fletcher H.; Lee, John E.; Sweet, Richard D. Department of Psychiatry, New York Hospital-Cornell Medical Center, Westchester Division, White Plains, NY 10605 **Parkinsonism, L-dopa, and intelligence.** American Journal of Psychiatry. 130(12):1386-1389,1973.

Although many patients with parkinsonism undergo a significant amount of intellectual impairment, several investigators have observed an improvement in intellectual functioning during the first year of treatment with L-dopa. Upon reexamining subjects after 30 months of treatment, however, it is found that most of the patients do not maintain this improvement. The reasons for the decline are not yet clear, but probably involve the waning influence of L-dopa, the onset or progression of the intellectual impairment common to parkinsonism and the normal aging process, and the impact of other physical illnesses. 19 references. (Journal abstract)

175540 Andreani, G.; Montebelli, M. L.; Caselli, G. Ospedale Psichiatrico Provinciale di Ferrara, Ferrara, Italy **/Observations on the therapeutic activity of clopenthixol in psychiatry./** Osservazioni cliniche sull'attivita terapeutica del clopenthixolo in campo psichiatrico. Giornale di Psichiatria e di Neuropatologia (Ferrara). 98(3-4):505-520, 1970.

Clinical experiences in the treatment of 70 hospitalized patients suffering from different forms of psychosis, most of them chronic, with the piperazinic derivative of thioxanthine (clopenthixol N 746) or Sordinol, are reported. Daily dosage did not exceed 105mg, and administration was continued for long periods of time. Results were generally favorable. Improvement consisted of normalization of thought processes, behavior, and diminution of psychosensory disturbances. Excitement and depressive states showed equal improvement, the former in the form of good sedation, the latter in a normalization of mood and the disappearance of anxiety states. It is concluded that the drug has a double action, in that it acts as a sedative and an antipsychotic agent, placing it among the major neuroleptics. Side-effects at low dosages were rare. 20 references.

175628 Massa, A. no address **Tantu Pashan and Lucidril therapy in mentally retarded children.** Indian Practitioner (Bombay). 25(9):427-432, 1972.

Use of Tantu Pashan and Lucidril in the psychopharmacological treatment of mentally retarded children is discussed. The combined drug

treatment has been effective in the treatment of children with seizures and muscular spasms. Three groups of children were treated: very low intelligence children; those with some mental retardation or simple mental backwardness; and children with infantile encephalopathies. Most children showed intellectual, social and physical improvement. In general, facial expressions were livelier, younger children reacted better, seizures and myoclonic jerks were arrested, and attention, concentration and activity improved.

176011 Modell, Walter. Cornell University Medical College, New York, NY **Updating the sleeping pill.** Geriatrics. 29(2):126-132, 1974.

Some of the characteristics and causes of insomnia, and nondrug and drug therapy for its relief, are discussed. The pharmacologic characteristics, the time and duration of action, and the potential for hangover of the hypnotic drugs are among the aspects of drug therapy considered in detail. The hypnotics mentioned include barbituates, chloral hydrate, glutethimide, methaqualone, the higher alcohols, nonprescription hypnotics, tranquilizers, antidepressants, and combinations.

176431 Roger, B.-M. no address /**An account of the use of fluphenazine since the establishment of psychiatry as a separate discipline.**/ Bilan de l'utilisation de la fluphenazine depuis la creation d'un secteur psychiatrique. Annales Medico Psychologiques (Paris). 1(4):550-555, 1972.

The results of the use of Fluphenazine in its simple form, as well as in its timed-release form, on 60 patients, male and female, are tabulated by age, diagnosis, dosage, dates used, and results. Satisfactory results from the use of the drug were obtained in 44 of 60 cases presented. The drug was placed on the market in 1965, about the same time that psychiatry was established as a separate medical discipline in France, thus simplifying reliable tabulation of the results. The timed-release form of the drug is one of the more interesting ones, particularly for the treatment of schizophrenia. Management is relatively simple. It can be taken well and allows patients to stabilize in their usual surroundings. Without the drug, chances are good that the same patients would become the chronically ill. There is some evidence of relapse among those on the drug for long periods of time, to the point of seeming to have never been treated at all.

176454 Hattori, Takashi; Nomura, Junichi; Kariyama, Naoyuki; Inoue, Katsura. Mie Prefectural University, Department of Medicine, Japan **Experiment with Doxepin (sinequan) in treatment of depressive states.** Medical Consultation and New Remedies (Tokyo). 8(5):183-188, 1971.

The effect of doxepin (sinequan) on depression was studied, based on an experiment in which 30 patients with a relatively minor case of depression were treated with this drug (75 to 150mg/day) for 2 to 14 weeks. The results show this drug was effective on anxiety, irritation and sleep disturbance. The drug showed remarkable to moderate effect in nearly 80% of the patients (40%). This drug was effective for manic-depressives and reactive depressives, but insignificantly effective for neurotics. Minor side-effects, such as dry mouth and nausea, were observed in three patients. 3 references.

176456 Akabori, Fumihiko. Nissei Hosptial, Japan **Experience in the use of Serenal (oxazolam) in the field of pediatrics.** Medical Consultation and New Remedies (Tokyo). 8(10):89-90, 1971.

The effects of Serenal (oxazolam) on pediatric disturbances were studied. Eleven 3- to 9-year-old children with Nabelkoliken were orally treated with this drug (5 to 10mg/day) for 3 to 6 days. The symptoms disappeared within 3 days in five children, and within 7 days in the rest of the children. No side-effects were observed. Five 6 to 11-year-old children with autointoxication were orally treated with this drug (10mg/day) for 3 days preceded by hypertonic glucose transfusion therapy, and the symptoms completely disappeared within 3 days. Ten 4- to 12-year-old children with various neuroses were orally treated with this drug (10mg/day) for 3 to 7 days. Symptoms disappeared within 3 days in two children and within 7 days in the rest of the children, and no side-effect was observed. A 5- and a 9-year-old child with eneuresis were orally administered Serenal (10mg/day) for 7 days with no improvement.

176471 Mikejiri, Kenichi; Itoi, Kohkichi; Yamaura, Harutaka; Goto, Tetsuya. National Ogura Hospital, Department of Neuropsychiatry, Japan **Experience in the use of Sinequan (doxepin hydrochloride) in treatment of neurosis, depression and depressive states.** Medical Consultation and New Remedies (Tokyo). 8(10):183-191, 1971.

The therapeutic effect of Sinequan (doxepin hydrochloride) was studied in 24 19- to 60-year-old neurotic and depressive patients treated with this drug (30 to 150mg/day) for 2 to 91 days. The effect was measured by means of the Hamilton Anxiety Scale. The drug was remarkably to moderately effective in 64.7% of the patients with neurosis, 75% of the patients with reactive depression and 66.7% of the patients with endogenous depression. One patient with endogenous depression showed aggravation of depression and experienced akathisia, and treatment was terminated after 2 days. Side-effects, such as drowziness, dry mouth, fatigue, akathisia and constipation, were observed in four other patients and disappeared during the process of treatment. This drug was not only effective on depression, but was also effective on anxiety, tension, irritation, insomnia and autonomic nervous symptoms. 21 references.

176542 Karasumoto, Kenzo; Sasamoto, Seiichiro; Ito; Sususumu; Yamakage, Nori. Ebetsu General Hospital, Japan **Experience in the drug Horizon and psychiatric interview.** Medical Consultation and New Remedies (Tokyo). 8(10):211-217, 1971.

The effects of the drug Horizon on psychotherapeutic interview was studied in 41 mixed diagnosis 9 to 63-year-old mental patients who showed strong tension and resistance toward interviews. Ss were intravenoüsly treated with this drug in various doses and solutions. The drug was effective in all neurotics, easing tension, facilitating communication and decreasing complaints. These optimistic results were repeated in the depressive cases. Among the 10 schizophrenic patients, 50% showed improvement in emotion and interviewing attitude, acting out abnormal experience, and easing tension and inhibition. Horizon was effective in one of two children under 10-years-old in facilitating communication and was also effective in patients with mania, epilepsy, atypical psychosis, alcoholic psychosis, psychopathic personality and juvenile paresis. Horizon induced emotional stability and relaxation with little abnormal physiological effect.

176564 Fujimoto, Akira; Nagasaka, Goro; Yamada, Etsuhide; Yorioka, Nobuyuki; Kobayashi, Kota; Saito, Yoshiko; Yoshida, Kazuo; Takahashi, Yukiya. Asakayama Hospital, Japan **Clinical experiences with a new psychotropic drug, R-6238 (pimozide).** Medical Consultation and New Remedies (Tokyo). 9(9):1987-2003, 1972.

Results of the use of a new psychotropic drug, pimozide, are extensively tabulated by degree of improvement when used with different disorders, degree of improvement in terms of maximum dosage, improvement in terms of length of disease, side-effects found when used for different disorders, age, sex, blood analysis, liver functions, urinalysis, EKG, EEG, blood pressure, and bodyweight. The drug was effective in 21 of 33 cases of schizophrenia (63.6%) and had no effect in 10 cases (30.3%). Two cases worsened (6.1%). Efficacy was excellent when used independently, but the general impression gathered from the study is that the psychotropic effect is more pronounced when used in combination with a tranquilizer. Side-effects included insomnia and extrapyramidal symptoms, controllable with tranquilizers. 11 references.

176582 Salan, R.; Gardjito, S. O. Department of Health, Djakarta, Indonesia **/Clinical trial with Nozinan R. at several mental hospitals in Java./** Clinical trial dengan Nozinan R dibeberapa rumah sakit djiwa di Djawa. Indonesian Psychiatric Quarterly (Djakarta). 4(2):35-42, 1971.

Results of a clinical trial of Nozinan, a psychotropic drug classified as a tranquilizer, which, although not new, has only recently become available in Indonesia, are discussed. Six Javanese hospitals, between October 1969 and May 1970, used different dosages of Nozinan and antiparkinsonian medication as required on 404 patients, of whom 222 were men and 182 women. Results were evaluated on a scale ranging from -1, condition worsened, to 3, excellent improvement (patient able to return to work and to adapt socially). Few alarming side-effects were witnessed. Two patients collapsed with lowered blood pressure, but revived without additional treatment. Nozinan treatment was most effective in paranoid and acute schizophrenic disorders, and more effective in acute cases than in chronic cases. The daily optimum dosage was 50 to 150mg. Dosages over 200mg showed a decrease in effectiveness.

176810 Kehne, Christine W. Hillcrest Childrens Center, Childrens Hospital, Washington, DC **Control of the hyperactive child via medication -- at what cost to personality development; some psychological implications and clinical interventions.** American Journal of Orthopsychiatry. 44(2):237-238, 1974.

In a paper presented at the 51st Annual Meeting of the American Orthopsychiatric Association, the use of medication in the treatment of hyperactive children and the child's and parents' attitudes toward such behavior control were discussed. The clinician must keep in touch with the feelings of the patient and the parents before and at the onset of the medication regime. With appropriate clinical intervention, there need not be appreciable negative effects upon personality development and healthy family patterning. Brief case vignettes illustrate forms of intervention found useful to the vast majority of hyperactive children. Some of the psychological issues implicit in chronic drug use are also discussed. (Journal abstract modified)

177320 Brown, Colin R.; Shroff, Phyliss F.; Forrest, William H., Jr. Department of Anesthesia, Stanford University School of Medicine, Palo Alto, CA **The oral hypnotic bioassay of hydroxyzine and pentobarbital for nighttime sedation.** Journal of Clinical Pharmacology. 14(4):210-214, 1974.

In a four point biologic assay of a complete randomized block design, the hypnotic effects of 50mg and 150mg hydroxyzine were compared with 60mg and 180mg of a standard drug, pentobarbital, in male patients from the medical and surgical wards of a Veterans Administration hospital. Effects were evaluated on the basis of patient's responses to four questions asked by specially trained nurses regarding the quality of sleep, time taken to fall asleep, comparison of sleep with that obtained in the home environment, and total length of sleep. For three out of four responses, the two doses of hydroxyzine showed effects not different from each other and similar to those of the low dose of pentobarbital. For effects on duration of sleep, 100mg hydroxyzine was approximately equal to 100mg pentobartibal. Sleepiness was the most common side-effect for both drugs. 13 references. (Author abstract)

177373 Cohen, Sidney; Ditman, Keith S. Dept. of Psychiatry, Neuropsychiatric Institute, Univ. of California, Los Angeles, CA **Gerovital H3 in the treatment of the depressed aging patient.** Psychosomatics. 15(1):15-19, 1974.

The use of Gerovital H3 (GH3) in the treatment of the depressed aging patient is reported. GH3 was tested in Ss suffering from either primary depression or as a symptom secondary to medical problems and it was hypothesized that selective amine oxidase inhibition would raise synaptic norephrine while avoiding the side-effects of broad spectrum monoamine oxidase inhibitors. Of the 41 Ss, 17 were classed as normals, 17 as psychiatric patients and seven had major medical problems. None of the normal Ss reported any side-effects and only two of the psychiatric Ss reported complaints none of which could be related to specific drug reactions. Of the normal Ss, 15 reported improvements in one or more of the following areas: sense of well-being, relaxation, sleeping time, energy or libido. Case reports are included. 5 references.

177511 Maskin, Michael B.; Riklan, Manuel; Chabot, David. Department of Psychology, California State College, San Bernadino, 5500 State College Parkway, San Bernadino, CA 92407 **Effects of 'short-term' versus 'long-term' L-dopa therapy in Parkinsonism on critical flicker frequency.** Perceptual and Motor Skills. 38(2):455-458, 1974.

Shorter and longer range effects of L-Dopa therapy in parkinsonism on critical flicker frequency (CFF) scores were investigated. Results indicate that the control group scored significantly higher on CFF, indicating superior neural integration when compared with the short-term or long-term L-Dopa group; the short-term L-Dopa group scored significantly higher than the long-term L-Dopa group, demonstrating better cerebral efficiency. It is suggested that a peculiar clinical state interfering with neural transmission may develop in parkinsonian patients on L-Dopa therapy prolonged 2 years or more. 10 references. (Author abstract modified)

177569 Fujita, Shizuyo; Kobayashi, Isao. Toyohashi, Shimin Byoin, Japan **Clinical effect of a new psychotropic drug, doxepin hydrochloride, in the treatment of depressive states.** Medical Consultation and New Remedies (Tokyo). 8(4):97-104, 1971.

The clinical effect of a new psychotropic drug, doxepin hydrochloride, in the treatment of depressive states is discussed. In an experiment, 15 patients with depression and 15 neurotic patients with anxiety were treated with this drug for a period from 7 days to 3 months. This drug was effective in 73.3% of the patients. The effect most frequently appeared 8 to 14 days after the beginning of treatment. Side-effects, such as fatigue, drowsiness, dry mouth, and insomnia were observed. 3 references.

177670 Turek, I. S. Maryland Psychiatric Research Center, Baltimore, MD 21228 **Combined use of ECT and psychotropic drugs: antidepressives and antipsychotics.** Comprehensive Psychiatry. 14(6):495-502, 1973.

Combined use of ECT and psychotropic drugs in schizophrenia and depression is discussed. Many patients in both diagnostic categories are not responsive and are treatment resistant. Although there is no theoretical justification, observed spectacular and long-lasting recoveries in some individual cases of chronic schizophrenia should compel the therapist to try ECT and psychotropic drug combinations. The combination of ECT and antidepressives in depressive syndromes is advocated. ECT might be helpful to reverse the cholinergic predominance into the adrenergic one to be followed with tricyclic drugs which appear to be working in the same direction but suffering from a lag time before their peak therapeutic effect. 34 references.

177671 Gottschalk, Louis A.; Covi, Lino; Uliana, Regina; Bates, Daniel E. College of Medicine, University of California, Irvine, CA **Effects of diphenylhydantoin on anxiety and hostility in institutionalized prisoners.** Comprehensive Psychiatry. 14(6):503-511, 1973.

The effects of diphenylhydantoin on anxiety and hostility in institutionalized prisoners were investigated in a placebo - drug double-blind study. There were no significant differences between drug and placebo groups in the magnitude of anxiety or hostility scores. Findings confirm observations of several other investigators that diphenylhydantoin has a weak effect, as an antianxiety or antihostility agent, even when administered over a 6 month period to a group of aggressive, antisocial offenders. The relationship and relevance of psychological state scores derived from the content analysis of speech to manifest behavior is discussed. 38 references.

177778 Satterfield, James H.; Cantwell, Dennis P.; Saul, Ronald E.; Lesser, Leonard I.; Podosin, Robert L. Andrew Norman Research Center, Gateways Hospital Hyperkinetic Children's Clinic, 1891 Effie St., Los Angeles, CA 90026 **Response to stimulant drug treatment in hyperactive children: prediction from EEG and neurological findings.** Journal of Autism and Childhood Schizophrenia. 3(1):36-48, 1973.

A study of neurological examinations, EEG findings, and behavioral responses to methylphenidate treatment in 57 hyperactive boys, 5 to 10 years of age, is reported and discussed. Results indicate that subjects with minor neurological abnormalities in four or more categories responded with significantly more improvement to methylphenidate treatment than subjects without abnormalities. Subjects with abnormal EEGs had significantly more improvement than those with normal EEGs. A significant correlation was found between the degree of evidence of brain dysfunction obtained from EEG and neurological examinations and the probability of response to methylphenidate treatment. It is suggested that both neurological and EEG examinations play a significant role in the assessment of hyperactive children. 21 references. (Author abstract)

177975 Pelton, E. Williams, II; Chase, Thomas N. Neurology Unit, NIMH, Bethesda, MD **L-Dopa and the treatment of extrapyramidal disease. (Unpublished paper).** Bethesda, MD, NIMH, 1974, 90 p.

L-Dopa is reviewed in relation to the treatment of extrapyramidal disease, principally focusing on the function of central dopamine (DA) containing neural systems in view of their crucial role in mediating the effects of L-dopa on motor behavior. It was concluded that L-dopa remains the most effective approach to the symptomatic relief of Parkinson's disease. L-Dopa has also been found to benefit parkinsonian signs arising as a part of several other central nervous system disorders. Replenishment of central DA stores appears to be primarily responsible for the therapeutic efficacy of L-dopa. Although the precise mechanism by which L-dopa influences extrapyramidal function is not completely understood, available evidence suggests that the concept of neurohumoral replacement therapy may have relatively limited applicability to the treatment of brain disease. 350 references.

178193 Jus, K.; Jus, A.; Gautier, J.; Villeneuve, A.; Pires, P.; Pineau, R.; Villeneuve, R. Department de recherches, Hopital St-Michel-Archange, Quebec 5, Canada **/Study of the effect of certain pharmacological agents on tardive dyskinesia and the rabbit syndrome./** Etude de l'effet de certains agents pharmacologiques sur la dyskinesie tardive et le syndrome du lapin. Vie Medicale au Canada Francais (Quebec). 2(9):871-875, 1973.

The effects of certain pharmacological agents on tardive dyskinesia and the 'rabbit syndrome' were studied. Clinical and polygraphic studies on the influence of a single intravenous dose of benztropine mesylate, diazepam, or diphenylhydantoin, and of a single oral dose of d-l tryptophan, on tardive dyskinesia and the 'rabbit syndrome,' are discussed to show that benztropine mesylate was effective in the rabbit syndrome, but provoked only a brief decrease in muscle tone in tardive dyskinesia, that diazepam was effective in both, but provoked a simultaneous decrease in the alertness level, that diphenylhydantoin was effective in 50% of the tardive dyskinesia cases and ineffective in 'rabbit syndrome,' and that d-l tryptophan was ineffective in both conditions. The possible mechanisms of action of these drugs are discussed, and study of long-term diphenylhydantoin administration in tardive dyskinesia is in progress. 22 references.

178549 Elek, S. D.; Stern, H. Department of Medical Microbiology, St. George's Hospital Medical School, London SW1X 7EZ **Development of a vaccine against mental retardation caused by cytomegalovirus infection in utero.** Lancet. 1(7845):1-5, 1974.

Cytomegalovirus infection in utero, an important cause of mental retardation, is discussed. A live tissue culture adapted strain of the virus was tested in volunteers. The subcutaneous route of inoculation was successful in stimulating neutralizing and complement - fixing antibody production without important side-effects. It is suggested that the use of such a vaccine in adolescent girls would reduce the incidence of primary cytomegalovirus infection in pregnancy and thus eliminate fetal brain damage due to this cause. 34 references. (Author abstract modified)

178618 McLellan, D. L. University Department of Neurology, Institute of Neurological Sciences, Southern General Hospital, Glasgow, Scotland **The suppression of involuntary movements with tetrabenazine.** Scottish Medical Journal (Glasgow). 17(11):367-370, 1972.

Tetrabenazine, in 25 to 250mg doses, was administered to 31 patients with various extrapyramidal disorders to determine its ability to suppress involuntary movement over periods varying from 2 weeks to 15 months. Clinical assessment of the patients' disability before and after treatment confirmed that tetrabenazine effectively suppresses choreiform and ballistic involuntary movements, particularly those associated with Huntington's chorea and cerebrovascular disease. Side-effects were encountered frequently and a controlled study in which tetrabenazine is compared with other active drugs is now desirable. 13 references. (Author abstract)

178946 Collard, J.; Fraipont, J.; Dufrasne, M. Universite de Liege, Rue Saint-Laurent, 58, 4000 Liege, Belgium **The first long-acting ('Retard') thymoanaleptic or antidepressant: the time-released dibenzepine with prolonged action.** Arzneimittel-Forschung (Aulendorf). 23(4):537-545, 1973.

Time released dibenzepine with prolonged action is described as the first long-acting thymoanaleptic or antidepressant. The psychological value of a single dose on awakening is emphasized. A total of 44 outpatients and 21 patients studied under control conditions were Ss. Data are present on overall activity, symptoms, EEG, and ECG. Side-effects were mild and easily controlled. Effects on impulses and mood are described. It is concluded that the drug is effective in various depressive states and neuroses. 16 references.

178950 Robin, Jean-Paul. Hopital Santa Cabrini, Montreal, Canada /A **comparative study of diazepam and methocarbamol in the treatment of lombosciatalgias./** Etude comparative de la valeur du diazepam et du methocarbamol dans le traitement de certaines lombosciatalgies. Vie Medicale au Canada Francais (Quebec). 2(5):442-443, 1973.

The results of treating 28 patients suffering from low back pains are described. Individual symptoms are tabulated and the procedure used to arrive at diagnoses is explained. The patients, for purposes of treatment, were divided up into two groups of 14 each. One group, five men and nine women aged 24 to 67, was given methocarbamol, the other, nine men and five women aged 26 to 61, diazepam. A numerical point system was devised to score the results of the treatment. The system is detailed and resulting scores tabulated. It is concluded that the addition of a muscle relaxant to the treatment of acute low back pains can give better results if administered as soon as the ailment sets in. Results suggest that the use of diazepam yields better results under these conditions. 3 references.

180299 Setyonegoro, Kusumanto; Wibisono, Sasanto. Dept. of Psychiatry, Univ. of Indonesia,

School of Medicine, Djakarta, Indonesia **Haloperidol (Janssen) in the treatment of unselected institutionalized psychiatric patients.** Indonesian Psychiatric Quarterly (Djakarta). 5(1):100-107, 1972.

The effect of Haloperidol (butyrophenone), a tranquilizer, on the treatment of 197 unselected, institutionalized psychiatric patients was studied. Haloperidol was given in tablets of 0.5mg, three times a day, increased up to dosage effecting optimal clinical responses. Injections (2.5mg or 5mg intramuscularly) were given to uncooperative, or very agitated patients, usually at the beginning of therapy. In some cases, the liquid form (Haloperidol drops) was administered. Psychiatric evaluations were made at least once a week on target symptoms based on a modification of the Factor Construct Rating Scale (FCRS). Excellent improvement was shown by 62% of the patients who were judged ready for social adjustment outside the hospital setting; 29.5% showed some degree of moderate improvement; 2.6% became worse; and 5.9% showed no improvement. Significant improvements were most observable in alleviation of mental distortion (hallucinations, delusions), agitation and excitement, and hostility. Remarkable improvement in disorganized impaired association, emotional dullness and lack of initiative were also quite significant among many of the schizophrenics. Side-effects were mild to moderate and primarily extrapyramidal. 3 references.

180301 Taguchi, Kanzo; Watanabe, Shosuke; Ebara, Takashi; Iguchi, Kinya; Nakashima, Yoshihiko; Otsuki, Saburo. Department of Neuropsychiatry, Okayama University Medical School, Okayama, Japan **Lithium distribution between cerebrospinal fluid and serum of affective psychotic patients treated with lithium carbonate and its clinical response.** Medicine and Biology (Tokyo). 86(5):333-336, 1973.

The relationship between lithium distribution in psychotic patients treated with lithium carbonate and clinical response was studied, based on an experiment in which eight patients with manic-depression, seven with schizophrenia and three with mental retardation were treated with lithium carbonate with or without combined treatment with levomepromazine, chlorpromazine, minor tranquilizer, and/or antidepressants. No relationship between lithium concentration in cerebrospinal fluid and clinical response was observed.

180672 Balassa, M.; Deisenhammer, E. Wagner-Jauregg-Krankenhaus des Landes Oberosterreich, Linz, Austria **/First results obtained with a new anticonvulsant of the benzodiazepine series (clonazepam)./** Erste Untersuchungsergebnisse mit einem neuen Antikonvulsivum der Benzodiazepin-Reihe (Clonazepam). Wiener Medizinische Wochenschrift (Wien). 122(3):27-31, 1972.

Results of tests made of the anticonvulsive effect of Clonazepam on 40 patients in two groups are discussed. Group 1 (average age 46 years old) consisted of 16 badly demented women permanently committed to a mental institute. Clonazepam was administered three times a day in 2mg doses, and increased to 4mg three times a day if attacks continued. Group 2 had 24 patients (average age 16.2years old). Preparations in use were gradually replaced by Clonazepam. Dosage varied between 1mg and 12mg daily, depending on age and bodyweight. Good results were observed for grand-mal attacks with EEG foci and focal attacks, with the exception of psychomotor attacks. The latter form of attacks, as well as grand-mal attacks with strong general changes, or generalized paroxysmal discharges, were not favorably affected. Petit-mal attacks with generalized 3-c/s spike wave discharges were affected favorably. The transient sedative effect makes the drug unsuited for outpatient treatment. Administration of the drug is indicated when customary anticonvulsants fail in treating the above listed forms of attacks. 11 references.

180674 Tessmann, R. Neurologisch-psychiatrischen Fachklinik im St. Johannes-Hospital, Hagen-Boele, Germany **/Thoughts on treatment by private physicians of abnormal sex drives./** Gedanken zur Behandlung von sexuellen Triebanomalien in der arztlichen Praxis. Medizinische Welt (Stuttgart). 23(6):188-191, 1972.

Treatment of abnormal sex drives by private physicians is considered. The feasiblity of antiandrogenic treatment with a new drug, Cyproteronacetate, is discussed. The need for physicians prescribing the treatment, as well as for psychiatrists appearing as expert witnesses before the courts, to thoroughly examine personal views on the subjects of freedom and sexuality is emphasized. Only on the basis of their personal opinions will they be able to justify the opinion that treatment with cyproteronacetate is justified, and at the same time avoid misuse, or incorrect application. The drug is particularly suited for the treatment of exhibitionism and pedophilia; five case histories illustrate the point.

180676 Bock, Karl-Joseph. 6200 Wiesbaden-Kohlheck, Langendellschag 81, Germany **/Experience in the treatment of cerebral insufficiency and peripheral blood circulation disorders using the EP 50/100 experimental drug./** Erfahrungen uber eine Behandlung von zerebraler Insuffizienz und peripheren Durchblutungsstorungen mit dem Versuchspraparat EP 50/100. Medizinische Welt (Stuttgart). 23(8):273-275, 1972.

The results of studying the effectiveness of EP 50/100 (Danaden retard) in 102 older patients, and their subsequent observation for 1 year, are discussed to show that the drug is highly effective. The combination of beta-pyridylcarbinal and pyritinol exhibited a significantly broad effect, the two substances complementing each other in their action mechanisms. Blood circulation in the brain is improved, vascular resistance in the end flow area is decreased, and permeability of the blood-brain barrier improved, thus increasing the metabolic process, and the oxygen and glucose supplies. Patients exhibiting symptoms of impaired memory, lack of concentration, sleep disturbances, emotional instability, behavioral disorders, and depression showed significant improvement when given the drug. A side-effect of the preparation is a significant improvement in circulation disturbances in arms and legs, particularly for brachialgia nocturna and intermittent claudication. Diabetic metabolism remained undisturbed. Flushing was observed in four cases that had previously reacted negatively to treatment with nicotinic acid. There were no gastrointestinal complaints. 19 references.

180992 Loney, Jan; Ordona, Truce T. University of Iowa, Iowa City, IA **Cerebral stimulants and minimal dysfunction: some questions, some answers, and some more questions.** American Journal of Orthopsychiatry. 44(2):243-244, 1974.

In a paper presented at the 51st Annual Meeting of the American Orthopsychiatric Association, questions raised during a large scale search for predictors of children's response to Ritalin were discussed. The diagnosis and treatment choice may depend on which staff child psychiatrist was seen. In developing scales to rate clinical improvement, the standard of comparison varies and there is a tendency to attribute all changes in the child's behavior to the drug. Only 31% of the sample shows no side-effects, 44% in appetite or weight loss, and sleep disturbance in 32%. The question of when to use cerebral stimulants in children with minimal brain dysfunction remains a complex issue. (Journal abstract modified)

181388 Kumashiro, Hisashi; Shoji, Osamu; Hirata, Junichiro; Noma, Takuji; Suemitsu, Shigeru. Department of Neuropsychiatry, Fukushima Medical College, Fukushima, Japan **On the stuporous and hypomanic episodes associated with spike and wave in electroencephalogram.** Fukushima Medical Journal (Fukushima). 22(1/2):1-7, 1972.

Clinical observations following medication are described for a female patient who demonstrated stuporous and hypomanic episodes of 1 to 2 weeks between the ages 1 to 14 years. Administration of anticonvulsants improved the EEG paroxysm but did not control the episodic symptoms completely. Thioridazine and propericiazine controlled the symptoms comparatively well. Intravenous injections of amobarbital and diazepam transiently improved both EEG paroxysm and episodic symptoms. It was determined that stuporous and hypomanic episodes as a psychoparetical and confusional state can be caused by frequent epileptic discharges following simple stimulations as determined by a low threshold of EEG paroxysm. 13 references. (Journal abstract modified).

181590 Kuromaru, Shoshiro. Department of Psychiatry, Kobe University School of Medicine, Japan **Pain and emotion.** Journal of Japanese Psychosomatic Society (Tokyo). 12(6):413-415, 1972.

Emotional suffering in patients with central pain was studied to determine what kind of psychotropic drugs are most effective for the pain. Imipramine was found to be the most effective drug for central pain. It is suggested that pain may be a kind of sensory perception as well as an emotional reaction. (Author abstract modified)

12 PSYCHOTOMIMETIC EVALUATION STUDIES

176480 Kaplan, Jonathan; Stillman, Richard; Gillin, J. Christian; Wyatt, Richard J. W. A. White Bldg., NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Attempts to evoke tolerance to DMT in man. (Unpublished paper).** Washington, DC, NIMH, 1974. 1 p.

Repeated injections of N,N-dimethyltryptamine (DMT) in man were studied to determine if tolerance develops. DMT was administered intramuscularly, using a dosage of 0.7mg/kg twice daily for 5 consecutive days to six normal, male

subjects. None of the parameters measured changed over the 10 drug administrations. Even when a second injection of DMT followed the first by less than 3 hours, no decrease in drug effects as noted. The drug produced behavior similar in some respects to schizophrenic behavior but there were also significant differences. Visual distortions predominated, with marked inability to preserve a train of thought. However, subjects interacted with the experimenters appropriately at almost all times with few delusions. All subjects expressed a preference for being left alone during some part of the experience. (Author abstract modified)

177407 Haigler, Henry J.; Aghajanian, George K. Yale University School of Medicine, New Haven, CT **Lysergic acid diethylamide and serotonin: a comparison of effects on serotonergic neurons and neurons receiving a serotonergic input.** Journal of Pharmacology and Experimental Therapeutics. 188(3):688-699, 1974.

The responsivity of serotonergic neurons and postsynaptic neurons to LSD, was compared in raphe neurons and neurons in four areas (ventral lateral geniculate, amygdala, optic tectum, and subiculum) with an identified 5-HT input from the midbrain raphe nuclei tested for their response to microiontophoretically ejected and systemically administered LSD. Compared to the raphe, cells in these postsynaptic areas were relatively insensitive to microiontophoretic LSD. Raphe cells could be totally inhibited by LSD at ejection currents too low to have any effect on the postsynaptic neurons. In contrast, 5-HT was very nearly equipotent in depressing the firing of the presynaptic (raphe) cells and the postsynaptic cells. To determine if LSD has any indirect inhibitory effect upon raphe neurons via neuronal feedback, LSD was administered to animals with a mesencephalic - diencephalic transection. In these Ss, LSD still produced inhibition of raphe cells at doses comparable to those in control Ss. Raphe neurons are therefore more sensitive to inhibitory effects of LSD than are postsynaptic neurons, and the inhibitory effect of low LSD doses on the presynaptic (raphe) cells is caused by a direct inhibitory action, rather than by an indirect action via a neuronal feedback. 42 references. (Author abstract)

177681 Sheehan, David V. C. F. Menninger Memorial Hospital, Menninger School of Psychiatry, Topeka, KS 66601 **A review of the use of LSD for the patient near death.** Psychiatric Forum. 3(1):21-23, 1972.

The use of LSD in the treatment of terminal patients in pain is discussed. Such use is a psychological as well as physical aid to such patients. The analgesic effects of LSD, based on four factors, are discussed. Several studies are described regarding the use of LSD on terminal patients suffering from malignant disease. Results of these studies indicate that LSD is capable not only of improving the lot of terminal patients by making them more responsive to the environment and their families but also by enhancing their ability to appreciate the subtle and esthetic nuances of experience. The imagery they experience not only gives esthetic satisfaction and feelings of peace but also creates a new will to live and a zest for experience which, against a background of dismal darkness and preoccupying fear, produces an exciting and promising outlook. 7 references.

178064 Naranjo, Claudio. no address **New approaches to consciousness.** New York, Pantheon, 1973. 235 p. $6.95.

Experimental work in 1965-66, in Chile, using four lesser known psychedelics as occasional adjuncts to psychotherapy, is described. The four drugs used were MDA, MMDA, harmaline and ibogaine. Special emphasis is given to the emergence of peak experiences, states in which the sense of the meaningfulness of the world is intensely heightened. The theme of the relationship between modern Western psychotherapy and the process of personality change set in motion by traditional meditative disciplines underlies these experiments.

180123 Martinez, Jorge B.; Kornblit, Guillermo; Naj, Leopoldo. no address **/Psychopharmacology of hallucinogens./** Psicofarmacologia de los alucinogenos. In: Fontana, A., Psicoanalisis y cambio. Buenos Aires, Ediciones de la Flor, 1971. 292 p. (p. 15-46).

A detailed study of hallucinogens is presented, covering the biochemistry of hallucinogens, phenethylamine derivatives, indole derivatives, psilocybin, LSD-25, substances antagonistic to hallucinogens, tolerance and dependence, and toxic substances. Tables and structural diagrams of drugs are included. The etymological background and customary outlook regarding the term drug on the part of physicians and laymen is detailed.

180139 Fontana, Alberto E. no address **/Psychotherapy with hallucinogens./** Psicoterapia con alucinogenos. Buenos Aires, Editorial Losada S.A., 1965. 220 p.

A brief history of the use of hallucinogens and their evolution as a tool in psychotherapy is given. The structures, biochemical properties, and the effects of the following drugs on man are described: LSD-25, mescaline, psilocybin, and sernyl. Clinical research on group and individual psychotherapy with hallucinogens as an aid is presented. It is concluded that hallucinogens can be of great value in psychotherapy if they are used as an auxilliary to the therapy. Use of hallucinogens per se in therapy can lead to inconclusive treatment. 509 references.

180140 Fontana, Alberto E.; Shavelzon, Alberto. no address **/The dynamics of a group in psychotherapy./** Dinamica de un grupo que trabaja en psicoterapia. In: Fontana, A., Psicoterapia con alucinogenos. Buenos Aires, Editorial Losada S.A., 1965. 220 p. (p. 11-20).

The dynamics of the group in psychotherapy are examined. A number of doctors formed a group with the object of developing new methods to use with patients and to investigate new possibilities in therapy. Students of medicine joined the group and its characteristic functions became threefold: work, investigation, and teaching. Experiments with LSD25 were conducted twice yearly. It is concluded that the use of hallucinogens as an aid in psychotherapy together with the functions of the group is an advance in the techniques of psychotherapy. 16 references.

180141 Martinez, Jorge B. no address **/A history of the use of hallucinogens./** Resumen historico del uso de alucinogenos. In: Fontana, A., Psicoterapia con alucinogenos. Buenos Aires, Editorial Losada S.A., 1965. 220 p. (p. 23-37).

A historical review of the use of hallucinogens is presented. A list of the countries of origin of various hallucinogens is given. In the beginning, hallucinogens were used simply as therapeutic agents to ascertain the mobilization of the unconscious; the results of the treatment were dependent on the properties of the drug. Later many authors began to point out the necessity of combining intense psychotherapy with drugs, LSD25 in particular. Special attention is paid to the histories of peyote, teonanacatl, psilocybin, and LSD25. Many authors relating their personal experiences with drugs are mentioned; among these are de Toledo, Huxley, Cattell, Frederking. 40 references.

180142 Reynoso, Roberto M.; Fontana, Alberto E.; Kornblit, Guillermo A. no address **/The mechanisms of action of hallucinogens./** Biofarmacologia de los alucinogenos. In: Fontana, A., Psicoterapia con alucinogenos. Buenos Aires, Editorial Losada S.A., 1965. 220 p. (p. 41-83).

The structures, biochemical properties, and effects on man of hallucinogens are discussed. The following drugs are described: LSD25, mescaline, psilocybin, and sernyl. Effects of the drugs on cerebral metabolism, adrenaline level, glucose, liver, arterial tension, pulse, respiration, temperature, and urine excretion are considered. Possible relations between hallucinations, fantasies, changes in mood, and other reactions are investigated. Counteracting drugs and their dosages are mentioned, as are other drug combinations which might be used. It is concluded that although the results are far from being conclusive, they are promising as guides or aids in formulating new experiments. A comprehensive bibliography is given. 280 references.

180143 Fontana, Alberto E.; Reynoso, Roberto M. no address **/Individual psychotherapy with hallucinogens./** Psicoterapia individual con alucinogenos. In: Fontana, A., Psicoterapia con alucinogenos. Buenos Aires, Editorial Losada S.A., 1965. 220 p. (p. 87-136).

Individual psychotherapy with hallucinogens is discussed. The screening of a patient for psychotherapy with hallucinogens is described: setting the number and duration of sessions; setting the time period between the beginning of treatment and the first treatment with hallucinogens; evaluation of the actual state of the patient through a series of tests to ascertain whether the drug's effect might be more harmful than beneficial. The announcement of the first treatment with hallucinogens often causes many fantasies in the patient. Instructions given to the patient prior to the experiment, dosages administered, and the outcome of a first session with LSD are described by means of examples taken from various treatments. Child psychotherapy with hallucinogens is also described. 155 references.

180144 Fontana, Alberto E.; Gasparino, Alba M. no address **/The use of hallucinogens in group**

psychotherapy./ Uso de los alucinogenos en la psicoterapia de grupo. In: Fontana, A., Psicoterapia con alucinogenos. Buenos Aires, Editorial Losada S.A., 1965. 220 p. (p. 139-190).

The use of hallucinogens in group psychotherapy is described. Many phenomena occurring in psychotherapy with hallucinogens can also be observed in group psychotherapy without the aid of psychedelics. When hallucinogens are used, music and food are used as indexes of anxiety or depression levels. Children's groups, commuter's groups, and groups that are free of charge are described. The communication level of a group is analyzed. The relationship of the group to the therapist was studied. It is concluded that psychotherapy with hallucinogens is useful and effective. 14 references.

180145 Touyaa, Hector Jorge. no address **/Results of clinical research in psychotherapy with hallucinogens./** Resultados de nuestro trabajo clinico. In: Fontana, A., Psicoterapia con alucinogenos. Buenos Aires, Editorial Losada S.A., 1965. 220 p. (p. 193-216).

Statistics on the results of psychotherapeutic treatment with LSD25, Cy39, and mescaline are given. The statistics are subject to certain variables such as the absence of a control group undergoing a similar therapy without the use of the hallucinogens. A classification system based on the American Psychiatric Association's classification system is used to categorize the patients according to disorders. The most positive results were obtained with the group of addicts, while the least positive were obtained with the schizophrenic group. Statistic results of psychotherapy with the aid of hallucinogens done by other authors are also included. 4 references.

181461 Soskin, Robert A. Clinical Services Division, Maryland Psychiatric Research Center, Baltimore, MD **Short-term psychotherapy with LSD: a case study.** Journal of Religion and Health. 12(1):41-62, 1973.

A case history is presented to demonstrate the usefulness of short term psychotherapy with LSD in certain cases of emotional disorders, particularly depression. The outcome with a 48-year-old hospitalized patient resulted in feelings of increased optimism and confidence, as well as in the development of a new self-concept. The changes were particularly impressive since the patient had received pschoanalytically oriented therapy many years prior to hospitalization without making appreciable improvement. The main impact of the psychedelic experience is temporarily to suspend those psychological processes that provide structure and constancy to the individual's perception of self-image, environment, beliefs, and values in the normal state of consciousness. It enabled the patient to transcend the network of learned social judgments that had previously constituted his sense of individuality and allowed him to find his true self. Such therapy is likely to have the greatest applicability in intensifying and hastening the therapeutic process with patients who possess the most ego resources, and the many reported failures may be due to its use solely in patient groups that are characteristically minimally responsive to other forms of treatment, such as alcoholics and patients with deep seated characterological problems. 9 references.

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

175149 Knapp, Suzanne; Mandell, Arnold J. Department of Psychiatry, University of California at San Diego, La Jolla, CA 92037 **Short- and long-term lithium administration: effects on the brain's serotonergic biosynthetic systems.** Science. 180(4086):645-647, 1973.

Short-term treatment with lithium chloride stimulates the uptake of tryptophan and its conversion to serotonin by striate synaptosomes. Preincubation of striate synaptosomes with L-tryptophan and in vivo administration of L-tryptophan appear to act in a similar manner. Midbrain tryptophan hydroxylase activity is reduced in temporal continuity with the lithium induced activation of tryptophan uptake and conversion. By 10 days, conversion of tryptophan to serotonin in nerve endings becomes a joint function of the maintained increased uptake of tryptophan and a decreased level of tryptophan hydroxylase activity in nerve endings. The occurrence of this delayed alteration corresponds in time to the previously described axoplasmic flow rate for tryptophan hydroxylase. 21 references. (Journal abstract)

175219 Claridge, Gordon S.; Birchall, Paul M. A. University of Glasgow, Department of Psychological Medicine, Southern General Hospital, Glasgow G51 4TF, Scotland **The biological basis**

of psychoticism: a study of individual differences in response to dexamphetamine. Biological Psychology (Amsterdam). 1(2):125-137, 1973.

Comparisons were made of the effects of dexamphetamine and a placebo on the covariation between two flash threshold and skin conductance level in two groups of subjects with high scores on, respectively, the psychoticism (P) and neuroticism (N) scales of Eysenck's PEN inventory. Under placebo, as before, the covariation between the two experimental measures followed an inverted U in high N subjects; while in high P subjects a tendency to U-shaped regression was detectable though less clear. The effects of dexamphetamine were unexpected. In high N subjects two flash threshold and skin conductance was maintained but it became linear, apparently due to a paradoxical tendency for the drug to shift these individuals towards a lower level of autonomic arousal. In high P subjects the effect was to cause a complete dissociation between the two experimental measures, any tendency to U-shaped regression actually being eliminated, rather than exaggerated. It is suggested that dexamphetamine may not have been an appropriate drug to administer, though it was considered that indirectly the results did support the hypothesis that there is a distinctive, and perhaps particularly unstable, kind of central nervous organization underlying psychoticism. 11 references. (Author abstract modified)

175245 Zarate, Arturo; Jacobs, Lawrence S.; Canales, Elias S.; Schally, Andrew V.; De la Cruz, Antonio; Soria, Jorge; Daughaday, William H. Hospital Ginec Obstet No. 1, IMSS, Gabriel Mancera 222, Mexico 12 **Functional evaluation of pituitary reserve in patients with the amenorrhea-galactorrhea syndrome utilizing luteinizing hormone-releasing hormone (LH-RH), L-dopa and chlorpromazine.** Journal of Clinical Endocrinology and Metabolism. 37(6):855-859, 1973.

Functional pituitary reserve in 18 patients with the amenorrhea - galactorrhea syndrome was evaluated using luteinizing hormone - releasing hormone (LH-RH), L-dopa, and chlorpromazine. Gonadotropin release after administration of synthetic LH-RH varied widely from that seen in normal women to that below the normal range; however, cases with pituitary tumor exhibited the lowest responses or no responses to LH-RH. Prolactin release in response to drugs which normally either stimulate (chlorpromazine) or inhibit (L-dopa) its secretion, also varied widely regardless of the presence or not of a pituitary tumor. It is concluded that LH-RH is a reliable test to determine the pituitary reserve in cases of galactorrhea associated with amenorrhea. These results suggest that high prolactin levels associated with a deficient secretion of gonadotropin in response to LH-RH may be indicative of an underlying pituitary tumor, even in the absence of cellar enlargement. 10 references. (Author abstract)

176108 Veldkamp, W.; Straw, R. N.; Metzler, C. M.; Demissianos, H. V. Upjohn Co., Kalamazoo, MI **Efficacy and residual effect evaluation of a new hypnotic, triazolam.** Journal of Clinical Pharmacology. 14(2-3):102-111, 1974.

Triazolam 0.5and 1.0mg, flurazepam 30 mg, and placebo were compared in 23 normal male volunteers for hypnotic activity and residual effects. Sleep questionnaire results revealed triazolam to have significant hypnotic activity, with both doses showing some superiority over flurazepam on sleep induction time, quality of sleep, and duration. Tests used in measuring residual drug effect at 10, 13, and 16 hours after drug administration included digit - symbol substitution, card sorting, mood - feeling, and ocular convergence. All of these tests showed some significant differences between drug treatments and placebo. The EEG results revealed that after a single dose of flurazepam 30 mg, EEG changes could be observed at least 16.5hours later. Doses of Triazolam 0.5and 1.0mg appeared to be shorter acting in that they had less effect on the EEG at this time. 9 references. (Author abstract modified)

176254 Garelis, E.; Neff, N. H. Dept. of Psychiatry, Athens Univ. Medical School, Egnition Hospital, Athens, Greece **Cyclic adenosine monophosphate: selective increase in caudate nucleus after administration of L-DOPA.** Science. 183(4124):532-533, 1974.

Treatment with L-dopa is shown to have produced an accumulation of adenosine 3',5'-monophosphate (cyclic AMP) in the caudate nucleus of the rat. In contrast, no change in the amount of cyclic AMP in the cerebellum is shown. Accumulation of cyclic AMP in the caudate nucleus after administration of L-dopa was prevented by prior treatment with the inhibitor RA 4-4602. Results support the assumption that dopamine formed from L-dopa selectively activates striatal adenylate cyclase. The in vivo activation of adenylate cyclase after treatment with L-dopa may be a useful model for studying neu-

rological and psychiatric disorders thought to involve the dopaminergic system of the brain. 9 references. (Author abstract)

177335 Lovstad, Rolf A. Institute for Medical Biochemistry, University of Oslo, Karl Johans gt. 47, Oslo 1, Norway **Interaction of phenothiazine derivatives with human ceruloplasmin.** Biochemical Pharmacology (Oxford). 23(6):1045-1052, 1974.

Tranquilizing drugs of the phenothiazine class were oxidized to free radicals by human ceruloplasmin. The blue color of the enzyme was reduced by addition of phenothiazine derivatives. In the presence of reducing agents the rate of the ceruloplasmin catalyzed oxidation of phenothiazine derivatives was markedly increased. NADH was oxidized during the process, suggesting that the activating effect is due to a reduction of phenothiazine derivative radicals, which rapidly react with several reducing agents. The Vmax values for the four substrates investigated do not vary significantly. However, at lower substrate concentrations the rate of triflupromazine oxidation was considerably slower. Phenothiazine derivatives activate the enzymic oxidation of dopamine and dopa, probably by acting as a cycling intermediate between ceruloplasmin and catecholamine. 16 references. (Author abstract modified)

177729 Bianchi, Camillo; Tomasi, Laura. Research Laboratories, Istituto De Angeli, Milan, Italy **Central nervous system and autonomic nervous system effects of amantadine and of some standard anti-parkinson drugs.** Pharmacology. 10(4):226-237, 1973.

The activity of amantadine HCl, trihexyphenidyl HCl, ethopropazine HCl, atropine sulphate, mecamylamine HCl and L-dopa against effects provoked by nicotine injected intracerebrally (tremors, convulsions, loss of righting reflex) was studied. The antagonistic drugs were injected intraperitoneally or intracerebrally. The above mentioned drugs except L-dopa and atropine prevented nicotine manifestations when given intraperitoneally. Amantadine, atropine and mecamylamine, resulted active when given intracerebrally (trihexyphenidyl, ethoprapazine and L-dopa could not be tested). Effects provoked by oxotremorine were counteracted by atropine, trihexyphenidyl, ethopropazine but not by amantadine and mecamylamine. Trihexyphenidyl, ethopropazine and atropine had anticarbamylcholine activity and mydriatic activity. Amantadine and mecamylamine were inactive or almost inactive. 35 references. (Author abstract)

177730 Zetler, G.; Thorner, R. Institut fur Pharmakologie, Medizinische Hochschule Lubeck, D-24 Lubeck, Germany **Drug induced catalepsy as influenced by psychostimulants, apomorphine, L-Dopa, and yohimbine.** Pharmacology. 10(4):238-251, 1973.

The anticataleptic activity of d,l-amphetamine, phenmetrazine, cocaine, apomorphine, yohimbine, and L-dopa was determined in mice. Cataleptic states were produced using haloperidol, trifluoperazine, nicotine, paraoxon, and tetrabenazine. In general, the anticataleptic activites of amphetamine, phenmetrazine, cocaine and yohimbine were of the same order of magnitude, nicotine catalepsy being preferentially antagonized by amphetamine and yohimbine. L-dopa was anticataleptic only when the animals were pretreated with a monamine oxydase inhibitor (iproniazid), but failed to antagonize the trifluoperazine catalepsy. Apromorphine exhibited very weak anticataleptic activity and was completely inactive against nicotine catalepsy. 59 references. (Author abstract)

177736 Bowers, Malcolm B., Jr. Department of Psychiatry, Yale University School of Medicine, New Haven, CT **Amitriptyline in man: decreased formation of central 5-hydroxyindoleacetic acid.** Clinical Pharmacology and Therapeutics. 15(2):167-170, 1974.

5-Hydroxyindoleacetic (5-HIAA), homovanillic acid, L-tryptophan, and probenecid were measured following a probenecid - tryptophan tolerance test in lumbar cerebral spinal fluid (CSF) treatment with amitriptyline (ami). CSF 5-HIAA levels were lower during this treatment despite high CSF L-tryptophan levels. Probenecid values were comparable before and during treatment. The results suggest that during clinical treatment with ami, central 5-hydroxytriyptomine turnover is decreased by a mechanism that does not involve decreased central availability of tryptophan. 23 references. (Author abstract)

177826 Angrist, Burton M.; Wilk, Sherwin; Gershon, Samuel. Neuropsychopharmacology Research Unit, Dept. of Psychiatry, New York University Medical Center, New York, NY **The effect of probenecid and large dose amphetamine administration on cerebrospinal fluid homovanillic acid.** Biological Psychiatry. 8(1):113-114, 1974.

The effects of amphetamine combined with probenecid on levels of certain amine metabolites in the cerebrospinal fluid were studied. The subject was a 36-year-old amphetamine abuser who volunteered to ingest both amphetamine and probenecid and to undergo lumbar puncture. Probenecid administration induced nausea but no vomiting on two occasions. Amphetamine administration induced a mild paranoid state. Probenecid alone increased homovanillic acid (HVA) levels in CSF without affecting 3-methoxy-4-hydroxy phenyl glycol levels. The further increase in HVA noted after probenecid and amphetamine were given concomitantly indicates increased dopamine turnover after amphetamine administration. 8 references.

178787 Bechtereva, N. P.; Bondartchuk, A. N.; Gretchin, V. B.; Iliukhina, V. A.; Kambarova, D. K.; Matveev, Yu. K.; Petushkov, E. P.; Pozdeev, V. K. Institute for Experimental Medicine, Kirovsky 69/71, Leningrad, USSR **Structural-functional organization of the human brain and the pathophysiology of the parkinsonian type hyperkineses.** Confinia Neurologica - Borderlands of Neurology (Basel). 34(1-4):14-17, 1972.

The multiple aspect investigation started and accomplished in 30 parkinsonian patients treated with the aid of multiple internal electrodes is discussed. Examination of the patients was undertaken to provide reasons for therapy and evidence on the structural - functional organization, as well as physiology and pathophysiology, of the human brain. Results of these studies provided data for a preliminary chart of functional interrelations between series of thalamic nuclei and between them and other cerebral subcortical structures in parkinsonian patients against the background of antiparkinsonian drugs. The evoked potential method made it possible to reveal the dynamics of interrelation between some subcortical structures occurring after cessation of antiparkinsonian drugs.

178817 Stancak, Andrej. Psychiatric Clinic of the Faculty of Medicine, Kosice, Czechoslovakia **Contribution of psychopharmacology to the psychophysiological theory of emotions.** Studia Psychologica (Bratislava). 14(3):203-207, 1972.

Contribution of psychopharmacology to the psychophysiological theory of emotions is discussed in terms of the peripheral, thalamic, central, and Papez's theories of emotions, which tend to localize emotions to certain structures of the brain as in the mesodiencephalic and the limbic system. Hypotheses on the effect of neuroleptics, chlorpromazine, and reserpine on the CNS are discussed. Hypotheses of the adrenergic nerve blockade and of the inhibition of the mesodiencephalic system and amygdaloid complex activity are compared with the reserpine hypothesis on the blockade of adrenergic activity. The catecholamine theory and its contribution to a better knowledge of emotional processes is discussed in light of the recent knowledge about the effect on the CNS of antidepressive drugs in the MAO group and the thymoleptics. The theory proposes a causal association between changes of mood, depressed and euphoric, and the decrease or excess of catecholamines, especially of noradrenaline in the brain stem. The effect of alcohol on emotions is also presented. 24 references. (Journal abstract modified)

179022 Eschenhof, E. Abteilung fur Experimentelle Medizin, F. Hoffmann La Roche & Co., AG, CH-4002, Basel, Switzerland /**Investigations on the fate of the anticonvulsant clonazepam in the organism of man, rat and dog.**/ Untersuchungen uber das Schicksal des Antikonvulsivums Clonazepam im Organismus der Ratte, des Hundes und des Menschen. Arzneimittel-Forschung (Aulendorf). 23(3):390-400, 1973.

Pharmacokinetic investigations with clonazepam in man, and metabolic studies with 14C labelled and nonradioactive clonazepam in man, rat and dog are reported. Methods used to determine clonazepam compounds were radiometry of the unchanged drug and of total concentrations; clonazepam metabolites in the urine were isolated and identified by means of enrichment and desalinization with amberlite XAD-2, extraction, thin layer chromatography, and mass spectrometry. Results are expressed in maximum content in human plasma, concentration mean values, bioavailability, absorbability, elimination half-lives, excretion rate, renal excretion half-lives, and metabolites of clonazepam. Clonazepam biotransformations in man and rat coincide, but there are marked deviations in the dog. (Journal abstract modified)

179023 Strasser, H.; Muller-Limmroth, W. Institut fur Arbeitsphysiologie der Technischen Unvers itat Munchen, 8 Munchen 40, Barbarastr. 16/I, Germany /**Central nervous stimulant induced physiological and performance changes in adults during sustained psychomotor tracking.**/

Physiologische Veranderungen und Regelleistungsverhalten alterer Probanden wahrend kontinuierlicher Tracking-Tatigkeiten nach Zufuhr einer zentral aktivierenden Substanz. Arzneimittel-Forschung (Aulendorf). 23(3):406-415, 1973.

An investigation into the effects of a central nervous system stimulant and placebo on tracking behavior and psychological parameters was conducted. Measures of skilled performances in adaptive and fixed tracking tasks were recorded for 10 males, before and after administrations of pemoline and placebo. Pemoline had increasingly more stimulating effects. There were no significant improvements after placebo except for deteriorations, as mental stress of the tracking tasks caused fatigue. Drug responses in tracking performances reflected distinctly in psychological parameters: instantaneous heartrate changes under pemoline were in the expected direction of significant relative increase compared with that of placebo. In arrhythmia, as a sign of acceptance of the challenge for human motor activity, fatigue antagonizing influences of pemoline become apparent. 43 references. (Journal abstract modified)

179987 Sellers, Edward M.; Koch-Weser, Jan. Clinical Pharmacology Program, Addiction Research Foundation, 33 Russell St., Toronto, Canada **Binding of diazoxide and other benzothiadiazines to human albumin.** Biochemical Pharmacology (Oxford). 23(3):553-566, 1974.

The binding of seven benzothiadiazines to human albumin was studied by equilibrium dialysis. All these 1,2,4-benzothiadiazine-1,1-dioxide analogs are highly bound to human albumin. The unsubstituted benzothiadiazine nucleus is bound less than the substituted analogs. Addition of a chlorine at C-6 and C-7 markedly increases binding, but further addition of methyl or sulfamyl groups results in some reduction of binding. Binding studies on benzothiadiazines do not demonstrate independent binding sites on albumin. Binding of drugs to albumin can be evaluated by fitting a logistic function to the experimental points with a least squares method. Diazoxide, the 7-chloro-3-methyl analog, was used for detailed investigations into the mechanism of protein binding of the benzothiadiazines. The effects of pH, temperature, ionic strength, cations and deuterium on the binding of diazoxide to human albumin indicate that the drug is bound mainly by hydrophobic interaction and to a lesser extent by hydrogen bonding. Difference spectroscopy studies show a shift in the electron distribution of diazoxide with binding. 49 references. (Author abstract)

179988 Belin, Marie-Francoise; Chouvet, Guy; Pujol, Jean-Francois. Departement de Medecine Experimentale, Universite Claude-Bernard-Lyon I, 8, avenue Rockefeller-69373 Lyon Cedex 2, France /**Transport of synaptosomal tryptophan and cerebral tyrosine: increase in the speed of uptake of reserpine or the inhibition of monoamine oxidase.**/ Transport synaptosomal du tryptophane et de la tyrosine cerebrale. Stimulation de la vitesse de capture apres reserpine ou inhibition de la monoamine oxydase. Biochemical Pharmacology (Oxford). 23(3):587-597, 1974.

Transport of tryptophan (Trp) and tyrosine (Tyr) across synaptosomal membranes was studied in vitro after administration of reserpine or monoamine oxidase inhibitor (IMAO). A long lasting stimulation of the high and low affinity uptake of the two amino acids was observed in different brain structures. Moreover, no direct effect of these drugs was observed in vitro. Kinetic study of the high affinity systems showed different mechanisms of regulation for Trp and Tyr uptake after reserpine administration. According to these results the increase of cerebral amounts of Trp and Tyr after reserpine or IMAO treatment previously described could be induced by a stimulation of transport of these amino acids by central nerve endings. However, the mechanism or inducing factors of these regulations remain unknown. 42 references. (Author abstract)

179989 Dybing, Erik. The Institute of Pharmacology, University of Oslo, Blindern, Oslo 3, Norway **Effects of chlorpromazine and actinomycin D on uptake and incorporation of certain amino acids, hypoxanthine and thymidine in cultures of human skin epithelial cells.** Biochemical Pharmacology (Oxford). 23(3):705-711, 1974.

The effects of chlorpromazine (CPZ) and actinomycin D on uptake and incorporation of certain amino acids, hypoxanthine and thymidine in cultures of human skin epithelial cells were studied. CPZ inhibited the uptake and incorporation of alanine, the uptake of alpha-aminoisobutyric acid (AIB), and the uptake and incorporation of hypoxanthine into acid soluble and insoluble fractions of human skin epithelial cells grown in culture. The uptake of phenylalanine and 1-aminocyclopentane-1-carboxylic acid was not inhibited by CPZ in the same dose range, but CPZ inhibited the incorporation of phenylalanine into acid insoluble material with 50% inhibition. Actinomycin D stimulated the uptake of thymidine into the acid soluble fraction of the HE-cells andincreased the

uptake to 160% of the controls. The uptake of hypoxanthine was inhibited by actinomycin D. Actinomycin D did not alter the uptake of AIB or cycloleucine. 9 references. (Author abstract modified)

179996 Holden, E. Michael; Brody, Jacob A.; Chase, Thomas N. National Institute of Neurological Diseases and Stroke, Federal Bldg., Room 10C08, Bethesda, MD 20014 **Parkinsonism-dementia of Guam: treatment with levodopa and L-alpha-methyldopahydrazine.** Neurology. 24(3):263-265, 1974.

Combined therapy in patients with parkinsonism-dementia of Guam with levodopa and L-alpha-methyldopahydrazine is discussed. This treatment has a considerable advantage over treatment with levodopa alone. The combined medication was given to 10 such patients for 2-18 months. Extrapyramidal features improved in all, and the improvement persisted or increased over time, usually with a diminishing dosage requirement of levodopa. Compared with previous experience with treatment with levodopa alone, the combined therapy: 1) shortened the time needed to reach maximal therapeutic effect; 2) greatly reduced gastrointestinal side-effects, thus permitting all patients to tolerate optimum therapeutic dosages; and 3) appeared to allow easier control of hypotension and induced dyskinetic and athetoid movements. 13 references. (Author abstract)

180047 Rimon, Ranan; Puhakka, Pertti; Venalainen, Eino; Mandell, Arnold J. no address **Choline acetyltransferase activity in the cerebrospinal fluid of psychiatric patients.** In: Psychiatria Fennica. Helsinki, Helsinki University Central Hospital, 1973. 301 p. (p. 265-267).

The activity of choline acetyltransferase (ChAc) was measured in the cerebrospinal fluid (CSF) of psychiatric patients who either had or had not received prior treatment with neuroleptic drugs. Drug treated patients with schizophrenia, depression, and organic brain syndrome reflected significantly less ChAc activity in CSF than nondrug treated patients. No relationship was demonstrated between the activity of the enzyme and any particular psychiatric syndrome. It is suggested that ChAc activity may be a useful chemical parameter in other CSF studies. 13 references.

181392 Coleman, Mary P. St. Joseph Hospital, Lancaster, PA **Oral 5HTP in primary autism with 5HT binding defect.** Psychopharmacology Bulletin. 10(1):64, 1974.

Blood platelet studies on the level of 5-hydroxytryptamine are described in eight patients with primary infantile autism. Earlier findings that 5-hydroxytryptamine was not bound well inside the platelets of autistic children suggest that a 5-hydroxytryptamine binding deficiency is a means of diagnosing this form of autism. The goal of the current project is to determine a means of treating this disorder by the administration of an amino acid.

181398 Vesell, Elliot S. Pennsylvania State University, Hershey, PA **Psychopharmacologic agents: effect on drug metabolism.** Psychopharmacology Bulletin. 10(1):67, 1974.

Drug metabolism studies of pharmacological interaction of a number of commonly used psychotherapeutic agents are described. Initial studies focus on effects of one drug on the metabolism of another. Drugs under study include phenobarbital, imipramine, amitriptyline, hydroxyzine, meprobamate, diazepam, thioridazine, promazine, trifluoperazine, chlorpromazine, and phenelzine. Levels of antipyrine in the subjects' blood plasma, measured weekly, provide an index of the metabolic interaction caused by the daily administration of the various psychopharmacological agents.

181588 Sawada, Hideo; Fukumoto, Mamoru; Yano, Hiroko; Hara, Akira; Kido, Akira. Department of Legal Medicine, Gifu University School of Medicine, Japan **Studies on metabolism of bromazepam (III): absorption, excretion, and metabolism of bromazepam in man.** ACTA Scholae Medicinalis Universitatis in Gifu (Gifu). 20(6):619-632, 1972.

The absorption, excretion, and biotransformation of bromazepam (BZ) were studied in man. Significant difference was observed in cumulative excretion of BZ, ABBP and 3-OH ABBP according to sex. Almost all of it was excreted within 24 hours in males; however, in females, the excretion was more gradual in comparison with that in males. After the single oral administration of 20mg BZ, changes of blood concentration of BZ with the passing time were observed in each of four cases of both sexes. 9 references. (Author abstract modified)

181811 Fernandez, J.; Browne, I. W.; Cullen, J.; Brennan, T.; Matheu, H.; Fischer, I. St. Brendan's Hospital, Dublin 7, Ireland **LSD...an in vivo retrospective chromosome study.** Annals of Human Genetics (London). 37(1):81-91, 1973.

In a single-blind retrospective in vivo study, chromosome analyses were performed on 32 psychiatric patients who had been treated with known amounts of pure d-LSD 25 and on 32 controls. The control group consisted of psychiatric patients who were on comparable psychopharmacological medication (other than LSD). The proportions of chromosomal aberrations noted in the two groups showed a nonsignificant difference. There was no cytogenetic evidence to suggest that pure d-LSD 25 given in therapeutic amounts produced increased chromosomal damage. 39 references. (Author abstract)

181879 Whitehead, W. E.; Renault, P.; Schuster, C. R. University of Cincinnati, Cincinnati, OH **Increased gastric acid during shock avoidance in man.** Psychophysiology. 11(2):222, 1974.

In a paper presented at the Thirteenth Annual Meeting of the Society for Psychophysiological Research, the effects of Sidman avoidance schedule on gastric acid secretion were studied in three women. Acid secretion was measured by continuously aspirating gastric secretions during a 1 hr avoidance session and a 1 hr postavoidance period. Compared to no shock sessions at the same time of day, avoidance increased acid secretion to approximately twice baseline values in all Ss. Acid secretion remained high and at about the same levels during the postavoidance period. Increases in acid secretion were independent of number of shocks received, the largest increase occurring in a session in which the S received no shocks. Chlorpromazine at 75 to 100mg prevented schedule induced increases. The data suggest that stressful work schedules contribute importantly to the development of peptic ulcer. This model may prove useful in evaluating tranquilizers and other drugs given to reduce gastric secretion. (Journal abstract modified)

181887 Cohen, M. J.; Rickles, W. H., Jr. University of California School of Medicine, Los Angeles, CA **Marijuana diminishes GSR activation peaking.** Psychophysiology. 11(2):225, 1974.

In a paper presented at the Thirteenth Annual Meeting of the Society for Psychophysiological Research, the acute effects of marihuana and past usage history of marihuana on learning and recall were studied. Ss with a history of either heavy or light marihuana usage were seen on two occasions, 7 days apart. In each usage category 4 groups were asked to learn a list of 9 paired-associates on day 1, and on day 2 recall the words and learn a second paired-associate list. Aside from measuring performance variables, phasic GSR was recorded. Results of an analysis of variance indicated a significant overall diminution of the phasic GSR for the heavy usage Ss compared to the lights. The post-hoc analysis of the interaction (Day : Peaking Points : Groups) demonstrated that marihuana diminished the magnitude of the GSR and activation peaking was present only on placebo days. On marihuana days, the magnitude of the GSR was so small that no significant activation effect was seen. The data were discussed in terms of marihuana's effects on physiology and learning. (Journal abstract modified)

181918 Serafetinides, E. A. UCLA School of Medicine and VA Hospital, Brentwood, Los Angeles, CA **Electroclinical discrepancies in anti-anxiety drugs.** Psychophysiology. 11(2):236, 1974.

A discrepancy between physiological and behavioral effects of anti-anxiety drugs was examined in a paper presented at the Thirteenth Annual Meeting of the Society for Psychophysiological Research. Studies in chronic alcoholic patients have shown that ethanol and chlordiazepoxide share a number of similar electrophysiological effects. They both increase the amount of fast activity and the frequency of the alpha rhythm in the EEG, as well as the abundance of EMG and GSR events. Such increases, compatible with physiological arousal, are in contrast with the behavioral effects of these two compounds, which are generally tranquilizing. This dichotomy is reminiscent of the altered pattern of sleep that hypnotic drugs induce and emphasizes the obvious but neglected fact that, as induced sleep differs from the naturally occurring one, so induced 'tranquility' differs from the normally present one, however the latter may be defined. (Journal abstract)

181958 Itil, T. M.; Marasa, J.; Bigelow, A.; Saletu, B. Missouri Institute of Psychiatry, University of Missouri School of Medicine, 5400 Arsenal St., St. Louis, MO 63139 **Prediction of neuroleptic effects of CI-686 based on quantitative pharmaco-electroencephalography: drug profiles**

and dose response curves based on computerized cerebral biorpotentials. Current Therapeutic Research. 16(1):80-95, 1974.

Quantitative pharmacoelectroencephalography using scalp recorded and computerized cerebral biopotentials was used in two double-blind studies. CI-686, a chromanamine derivative, produces significant effects on human brain function. The central nervous system (CNS) effects of CI-686 were dose related, and all but three dosages investigated could be statistically differentiated from placebo. The maximum effects of CI-686 are seen 1 hour after oral administration. Based on the computer electroencephalograms (CEEG) profiles and the dose response curves it is predicted that CI-686 will have clinical effects similar to those seen after major tranquilizers (neuroleptics), that have strong sedative and few extrapyramidal side-effects, such as thioridazine and chlorpromazine. However, the effects of CI-686, compared to other neuroleptic phenothiazines, are characterized by an early onset, a relatively short duration, and, most importantly, a bipolar action. CI-686 shows after 1 hour a neuroleptic but 6 hours after administration, a central stimulatory CEEG profile. It is concluded that this drug has to be given more frequently than other major tranquilizers in order to have antipsychotic effects. 16 references. (Author abstract modified)

182166 Cushman, Paul, Jr. Department of Medicine, St. Luke's Hospital, New York, NY 10025 **Testosterone and luteinizing hormone (LH) in untreated and methadone maintained narcotic addicts.** Federation Proceedings. 32(3):694, 1973.

At the 57th annual meeting of the Federation of American Societies for Experimental Biology, testosterone and luteinizing hormone (LH) levels in untreated and methadone maintained narcotic addicts were reported. Sexual disturbances were common in male urban long-term narcotic addicts, especially potency, libido and delayed ejaculation. The possibility that these sexual symptoms may be related to sex hormones was examined in untreated addicts (A), abstinent exaddicts, long-term therapeutic community residents (EA), abstinent addicts formerly maintained with methadone (AA), methadone maintained (MM) and normal controls. Histories, physical examinations, and blood for T, LH, and liver function tests as well as urine for methadone, morphine, etc.,were obtained on all patients. Twenty nine unselected MM patients, in treatment with 90mg for 20 months, had serum T of 510. Prospective study of 19 A before entry into methadone treatment showed their T to be 473 and LH of 10. After 3, 6 and 12 months (17 remaining in treatment), T was 494, 451 and 530 respectively. No change in mean LH was observed. (Author abstract modified)

14 MECHANISM OF ACTION: BEHAVIORAL

174994 Mendels, Joseph; Frazer, Alan. VA Hospital, University and Woodland Avenues, Philadelphia, PA 19104 **Brain biogenic amine depletion and mood.** Archives of General Psychiatry. 30(4):447-451, 1974.

The relationship between brain biogenic amine depletion and mood was studied. The behavioral effects of drugs that deplete the brain of biogenic amines were reviewed. Behavioral changes associated with reserpine administration were interpreted as being primarily a psychomotor retardation - sedation syndrome, due perhaps to a dopamine deficiency, and would not be an adequate model for clinical depression. In susceptible persons, particularly those with a prior history of depression, this psychomotor retardation - sedation might be sufficient to trigger a depression like episode. More selective amine depletion, produced by alpha-methylparatyrosine or by parachlorophenylalanine is not associated with depression, but these drugs produce a greater reduction in amine metabolite concentrations than that in depressed patients. It is suggested that the depletion of brain norepinephrine and dopamine, or serotonin, is, in itself, not sufficient to account for clinical depression. 90 references. (Author abstract modified)

175003 Galanter, Marc; Stillman, Richard; Wyatt, Richard J.; Vaughan, Tom B.; Weingartner, Herbert; Nurnberg, Fran Luckom. Albert Einstein College of Medicine, Bronx Municipal Hospital Center, Department of Psychiatry, Jacobi Hospital, Rm 118, Bronx, NY 10461 **Marihuana and social behavior.** Archives of General Psychiatry. 30(4):518-521, 1974.

The relationship between marihuana and social behavior was studied. Questionnaire responses from subjects in three 12 member sensitivity groups were analyzed and compared with responses given before the marihuana users participated in the groups. Although somatic sensory experiences and feelings of detachment were consistent in the marihuana condition, no consistent affective changes, increased insight, or increased

feelings of cohesiveness were experienced. These subject responses were at variance with those anticipated by subjects based on previous marihuana experiences, and were probably influenced by marihuana folklore. Marihuana in this context was found to act as a mild psychotomimetic, with no demonstratable effectiveness as an adjunct to group therapy or an antidepressant. 23 references. (Author abstract modified)

176109 Goldberg, Janice B.; Kurland, Albert A. Dept. of Psychology, University of Maryland, Baltimore County, MD **Pimozide in the treatment of behavioral disorders of hospitalized adolescents.** Journal of Clinical Pharmacology. 14(2-3):134-139, 1974.

The usefulness of pimozide in the management of patients with behavioral disorders was tested. Thirty male adolescents residing in a hospital for the mentally retarded received pimozide, at a dosage level ranging from approximately five to eight mg per day. After a period of 12 weeks of treatment, anxiety seemed alleviated and social behavior improved, although cognitive functioning was not significantly improved. Pimozide maintained subjects with behavior problems as well as did their prior medications, while a statistically significant number of placebo patients worsened. Pimozide produced limiting side-effects in two subjects although clinical laboratory findings indicated no toxicity. 7 references. (Author abstract modified)

176675 O'Brien, Charles P.; DiGiacomo, Joseph N.; Webb, William. Dept. of Psychiatry, University of Pennsylvania, Philadelphia, PA 19104 **Management of hostile, suspicious patients. Trifluoperazine versus haloperidol.** Diseases of the Nervous System. 35(2):75-78, 1974.

The use of trifluoperazine and haloperidol in the management of hostile, suspicious patients is investigated. When compared in double-blind fashion, the two drugs are equal in global clinical ratings. Haloperidol shows significantly more improvement on the Brief Psychiatric Rating Scale and on the Global Paranoia rating. On the Global Hostility rating and in speed of onset of activity, the effects of the two drugs are not significantly different. In a small subsample of extremely uncooperative patients, haloperidol showed marked effects, but trifluoperazine showed only minimal or moderate effects. 7 references. (Author abstract modified)

177318 Globus, G.; Phoebus, E.; Humphries, J.; Boyd, R.; Gaffney, D.; Gaffney, S. Department of Psychiatry and Human Behavior, California College of Medicine, University of California, Irvine, CA 92664 **The effect of lorazepam on anxious insomniacs' sleep as recorded in the home environment.** Journal of Clinical Pharmacology. 14(4):192-201, 1974.

The effect of the benzodiazepine lorazepam on sleep variables in a population of anxious insomniacs and control spouses was studied. Electrophysiological recordings were obtained in the home environment over a 5 week period. A tendency towards normalization of the sleep pattern of the insomniacs without suppression of REM sleep is reported. Home recording proved feasible and would seem preferable for certain research problems. 10 references. (Author abstract)

177450 El-Yousef, M. Khaled; Janowsky, David S.; Davis, John M.; Rosenblatt, Jack E. Department of Psychiatry, Vanderbilt University, School of Medicine, Nashville, TN **Induction of severe depression by physostigmine in marijuana intoxicated individuals.** British Journal of Addiction (London). 68(4):321-325, 1973.

The role of anticholinergic activity in marihuana's behavioral effects was evaluated through administering physostigmine to two marihuana intoxicated patients. In both cases physostigmine antagonized the marihuana high and induced a profound clinical depressive reaction. The reaction was antagonized by administration of 1mg atropine. 8 references. (Author abstract modified)

177674 Zeidenberg, Phillip; Clark, W. Crawford; Jaffe, Joseph; Anderson, Samuel W.; Chin, Susan; Malitz, Sidney. Department of Biological Psychiatry, New York State Psychiatric Institute, New York, NY **Effect of oral administration of delta9 tetrahydrocannabinol on memory, speech, and perception of thermal stimulation: results with four normal human volunteer subjects. Preliminary report.** Comprehensive Psychiatry. 14(6):549-556, 1973.

Quantitative measures of speech, memory, and thermal perception made simultaneously in subjects functioning under the influence of a fixed orally administered dose of pure delta9-tetrahydrocannabinol are reported. Subjects were less able to discriminate between a previously seen item and a new item under the influence of

the drug. The return toward normal after peak drug effect indicates that the observed phenomenon is not attributable to fatigue. The drug also interfered with short-term recognition memory. Unrehearsed extemporaneous speech was recorded immediately after completion of the lag recognition memory task in each round. The overall mean discrimination of thermal stimulation decreased under the effect of the drug. The persistence of diminished thermal discrimination may indicate that the analgesic effect of the drug is more prolonged than the cognitive effect. 12 references.

177716 Hartmann, Ernest; Cravens, James. Sleep and Dream Laboratory, Boston State Hospital, 591 Morton St., Boston, MA 02124 **The effects of long term administration of psychotropic drugs on human sleep: IV. The effects of chlorpromazine.** Psychopharmacologia (Berlin). 33(3):203-218, 1973.

The effects of the daily administration of chlorpromazine to normal young males aged 21 to 35 years is reported. Effects on laboratory recorded sleep, home sleep, and mood were studied. Chlorpromazine significantly increased total sleep and decreased waking, especially on the first days. Slow wave sleep, D-time, and the stages of sleep considered individually were unchanged. Chlorpromazine had considerable effects on home sleep and mood variables. There were increases in the tension - anxiety, anger - hostility, and fatigue factors of the Psychiatric Out-patient Mood Scale. What was most striking was the lack of effect of laboratory sleep measures in view of the effects on mood and home sleep reports. 33 references. (Author abstract)

177717 Hartmann, Ernest; Cravens, James. Sleep and Dream Laboratory, Boston State Hospital, 591 Morton Street, Boston, MA 02124 **The effects of long term administration of psychotropic drugs on human sleep: V. The effects of chloral hydrate.** Psychopharmacologia (Berlin). 33(3):219-232, 1973.

The effects of long-term administration of chloral hydrate on normal young males aged 21 to 35 years is reported. The effects on laboratory sleep, home sleep, and mood were investigated. Chloral hydrate significantly increased total sleep time and decreased sleep latency, the effects being greater on the early days of administration. There was no effect on slow wave sleep, D-time, or the stages of sleep studied separately. Chloral hydrate produced very little effect on mood or on subjective aspects of sleep, but it did produce distortion of the usual interrelationships between laboratory sleep and mood. It is concluded that chloral hydrate is not a placebo. The differences between various currently used hypnotic agents are discussed. 20 references. (Author abstract modified)

177718 Hartmann, Ernest; Cravens, James. Sleep and Dream Laboratory, Boston State Hospital, 591 Morton Street, Boston, MA 02124 **The effects of long term administration of psychotropic drugs on human sleep: VI. The effects of chlordiazepoxide.** Psychopharmacologia (Berlin). 33(3):233-245, 1973.

The effects of long-term administration of chlordiazepoxide (CDX) on normal young males aged 21 to 35 years is reported. The effects on laboratory sleep, home sleep, and mood were investigated. CDX produced an immediate increase in sleep time, but this returned to placebo levels after 2 to 3 days. Slow wave sleep was normal for the first few days, but then decreased and remained low. D-time similarly was not greatly affected for the first days, but is then decreased for the remainder of the 4 weeks on medication. During the period when both slow wave sleep and D-time are decreased, stage two sleep is increased. CDX produced little effect on mood; subjective sleep quality was judged better on CDX than on placebo. 28 references. (Author abstract)

177720 Roth, Walton T.; Tinklenberg, Jared R.; Whitaker, Charlotte A.; Darley, Charles F.; Kopell, Bert S.; Hollister, Leo E. Stanford University Medical Center, Stanford, CA 94305 **The effect of marihuana on tracking task performance.** Psychopharmacologia (Berlin). 33(3):259-265, 1973.

The error patterns of 19 young male subjects, mean age 20 years, who received placebo and 18 who received marihuana were compared in a 5 minute tracking task performed before and after the marihuana or placebo was given. After marihuana there was an increase in total errors as measured by standard deviation and mean deviation error scores. Although marihuana is reputed to create a fluctuating effect, under the conditions of this experiment the variability of error scores between successive 15 second time periods in the marihuana group was not significantly greater than in the placebo group. In addition the marihuana deficit did not show significant time

trends during the task. 15 references. (Author abstract modified)

177771 Winsberg, Bertrand G.; Press, Mark; Bialer, Irv; Kupietz, Samuel. Child Psychiatric Evaluation Research Unit, New York State Department of Mental Hygiene, 524 Clarkson Avenue, Brooklyn, NY 11203 **Dextroamphetamine and methylphenidate in the treatment of hyperactive/aggressive children.** Pediatrics. 53(2):236-241, 1974.

The comparative effectiveness of dextroamphetamine and methylphenidate for the treatment of severe behavior disorders among children hospitalized for neuropsychiatric conditions is reported. Findings indicate that both drugs attenuate hyperactive and aggressive behaviors and that children who respond to one may be expected to respond to the other. Side-effects were generally equally distributed between both medications and were of modest degree. One case each of methylphenidate induced dyskinesia and of dextroamphetamine induced psychosis is reported. The clinical implications of the findings are discussed, and directions are suggested for research on some of the observed clinical problems. 22 references. (Author abstract)

180065 Janke, W.; Debus, G. Department of Psychology, University of Dusseldorf, Dusseldorf, Germany **Double-blind psychometric evaluation of pimozide and haloperidol versus placebo in emotionally labile volunteers under two different work load conditions.** Pharmakopsychiatrie Neuropsychopharmakologie (Stuttgart). 5(1):34-51, 1972.

The effects of haloperidol and pimozide were examined in a battery of psychological tests on emotionally unstable volunteers. The effects of both drugs at both dose levels are dependent on the situation. Mainly with haloperidol there is a clear cut interaction between drug effects and low or high work load conditions. Under low work load conditions, haloperidol and pimozide produce emotional stabilization and amelioration of mood along with slight improvement of performance in some areas. Under high work load conditions the positive effects of haloperidol disappear and are partly reversed. The effects of pimozide, however, can be shown to be more resistant to the change of the experimental setting. 26 references. (Author abstract modified)

180155 Varma, L. P. Ranchi Mansik Arogyashala, Kanke, Bihar, India **Cannabis psychosis.** Indian Journal of Psychiatry (Madurai). 14(3):241-255, 1972.

A study at Ranchi Mansik Arogyashala examining 1248 cases of cannabis psychosis in males out of 39001 admissions to this hospital is reported. The group with cannabis psychosis excludes those cases where cannabis is merely incidental or a precipitating factor in the course of psychosis. The mean age of this psychosis is 35 years. The majority of patients come for treatment within 6 months of the onset of their illness. When a man shows manifestations of psychosis, he is usually confined to his room and is not allowed the opportunity of smoking marihuana and after a few days his symptoms disappear. He then mixes with his old friends and the cycle is repeated. Its incidence is significantly high among cultivators, laborers, and priests. Marihuana is used to relieve exhaustion and ease domestic worries. Most cannabis users are religious and believe that it brings them nearer to God. The clinical features of cannabis psychosis include: an anxiety state, then an acute toxic state, and then a mild state of excitement. The physical symptoms include emaciation, ruddy complexion, and dull eyes. The psychosis is episodic in nature and appears to be closely dependent on the intake of the drug. 21 references.

180699 Bernheim, J.; Michiels, W. Institut de Medecine Legale, 38, Boulevard d'Yvoy, CH-1205 Geneva, Switzerland **/Psychophysiological effects of diazepam (Valium) combined with a moderate dose of alcohol in man./** Effets psychophysiques du diazepam (Valium) et d'une faible dose d'alcool chez l'homme. Schweizerische Medizinische Wochenschrift (Basel). 102(24):863-870, 1973.

The effects of diazepam (Valium) combined with moderate ingestion of alcohol given separately or in association, on the behavior of 40 volunteer students aged between 20 and 30 years was studied. The subjects underwent various tests, i.e. time reaction (simple and choice), diffused attention, coordination of movements and statometry, and were then asked for a subjective assessment. Results show that administration of diazepam alone prolongs latency or response to the diffused attention test, slows performance of the movement coordination test and diminished steadiness in the standing position. Only the statometry test is appreciably modified by alcohol. Combination of diazepam and alcohol shows potentiation of ef-

fect in tests of audiovisual reaction time, diffused attention, and statometry. The more complex the task, the more it is affected. 10 references. (Author abstract modified)

181152 Saulle, Richard D. Dept. of Internal Medicine, Misericordia-Fordham Hospital Affiliation, Bronx, NY **Psychopharmacology of the cannabinoids.** Psychosomatics. 14(6):352-354, 1973.

Studies of the psychopharmacology of the active principles and metabolites, physico-chemical properties and biochemical modalities of action of cannabis derivatives are discussed and reviewed. The importance of research into the psychopharmacological properties of these agents is stressed in the light of their widespread use. Studies of effects in both humans and animals are reported. 12 references.

181270 Green, Richard S.; Rau, John H. Long Island Jewish -- Hillside Medical Center, P.O. Box 38, Glen Oaks, NY 11004 **Treatment of compulsive eating disturbances with anticonvulsant medication.** American Journal of Psychiatry. 131(4):428-432, 1974.

Treatment with anticonvulsant medicine (diphenlhydantoin) of patients with eating problems is reported. Most of the patients had failed to benefit from amphetamine dosages in the past. Three case reports for each of the patient groups of compulsive eaters are presented. Ten patients with symptoms of compulsive eating were treated pharmacologically with diphenlhydantoin. All but one had abnormal EEGs, indicating that neurological dysregulation may have been an etiological factor. Nine patients were treated successfully. It is suggested that compulsive eating may be a function of neurological disturbance, with psychodynamic factors determining whether patients become anoretic or obese or maintain their weight at normal levels. A rigorous double-blind placebo trial is also suggested. 26 references. (Journal abstract modified)

181393 Hartmann, Ernest L. Boston State Hospital, Boston, MA **Effects of drugs on sleep.** Psychopharmacology Bulletin. 10(1):64-65, 1974.

The effects of long-term administration of amitriptyline, chlordiazepoxide, chloral hydrate, chlorpromazine and reserpine in the laboratory sleep of 14 normal subjects were studied. Preliminary results indicate reserpine increases the amount of desynchronized or dreaming (D-time) but increases the time spent in other stages of sleep. With amitriptyline, the sleeper slept longer but had less D-time than he did under normal conditions. The other three drugs produced fewer changes in sleep patterns.

181394 Heise, George A. Indiana University, Bloomington, IN **Program in behavioral pharmacology.** Psychopharmacology Bulletin. 10(1):65, 1974.

An analysis of specific effects of scopolamine, atropine and d-amphetamine on stimulus discrimination, memory and learning is described. A variety of trial operant conditioning techniques have been developed for analyzing possible drug effects on behavioral processes in rats. Performance decrements observed after administration of these drugs was attributed to effects on registration and retrieval of discrimination events rather than on their storage.

181853 Ellis, M. J.; Witt, Peter A.; Reynolds, Ronald; Sprague, Robert L. Children's Research Center, University of Illinois, Champaign, IL 61820 **Methylphenidate and the activity of hyperactives in the informal setting.** Child Development. 45(1):217-220, 1974.

The range of dosages of methylphenidate which alter the activity of hyperactive children playing individually in widely spaced sessions in the same play setting was examined. From a photographic record, multiple measures related to activity and distractibility were derived and used to test the effects of 0.10, 0.30 and 1.00mg/kg of methylphenidate relative to that of a placebo. There were no discriminable effects. It is presumed that methylphenidate's action does not influence energy expenditure patterns but that its mode of action involves attentional mechanisms. Results show that methylphenidate seems to improve tractability and learning in situations involving clear cut task demands and high compliance, yet leaves informal behavior undisturbed. 13 references. (Author abstract modified)

181959 Roberts, Charles Dewitt; Sloboda, Walter. 5217 42nd St., N.W., Washington, DC 20015 **Afrodex vs. placebo in the treatment of male impotence: statistical analysis of two double-blind crossover studies.** Current Therapeutic Research. 16(1):96-99, 1974.

Afrodex was compared to placebo in the treatment of male impotence. Clinical studies per-

formed by Miller and by Sobotka to show the efficacy of Afrodex have been reanalyzed using the analysis of covariance. It was found that both involved essentially comparable groups of patients assigned to sequences of drug administration. Support for a significant treatment effect was found only in the Sobotka study. No carryover effect was found, thus reversing the conclusions of both authors. The models applied to the data were moderately efficient in explaining sources of observed variation. However, evidence is presented which suggests that the two studies cannot be legitimately pooled, although the analysis for this procedure is presented. 8 references. (Author abstract)

182118 Ogawa, Nobuya; Nakano, Shigeyuki. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Sapporo, Japan **Manifest anxiety and antianxiety drug effects in normal volunteers.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):114, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the relationship between anxiety level and the effect of antianxiety drugs was examined from the point of view of the state and trait concept of anxiety. Taylor's Manifest Anxiety Scale (MAS) was employed to measure trait anxiety. An increase of heartrate was found in the placebo group during instruction of test performance which was more prominent in the high anxiety (HA) group than in the low anxiety (LA) group . In a mirror drawing period, heartrate decreased to the initial level in the HA group, whereas the LA group maintained almost the same level as in an instruction period. In the benzodiazepine group both instruction and performance of the mirror drawing test induced an increase of heartrate. In group 3, BD-20mg reciprocal effects were obtained on heartrate change between HA and LA groups as compared to those of group 1 in two periods. These results suggest that antianxiety drugs produce different effects in trait anxiety and state anxiety. (Author abstract modified)

15 TOXICOLOGY AND SIDE EFFECTS

175459 Hildick-Smith, Marion. Department of Geriatric Medicine, St. Mary's Hospital, Etchinghill, Near Folkestone, Kent, England **The patient's view of L-dopa after one year's therapy.** Gerontologia Clinica (Basel). 15(2):74-83, 1973.

Parkinsonian patients under nonhospital L-dopa regime were studied to determine perserverance of the drug treatment. A selected series of 15 parkinsonian patients were examined before and after 14 months treatment while they were under minimal supervision. The purpose of this survey was to determine whether the patients continue with their drug treatment despite unpleasant toxic effects. It was discovered that the average dose taken during this period was 2g a day compared with 3.5g daily while in the hospital. Two of the older patients abandoned the L-dopa treatment altogether. Toxic effects and feelings of confusion were still reported in most of the subjects. Increased mobility and abnormal movements were noted. No serious pathological or ECG abnormalities were seen after long treatment with L-dopa in the cases suffering from postural blood pressure fall. The general practitioner can play a vital role by persuading the patient to continue the drug dosage. 24 references. (Author abstract modified)

175935 Davis, John M. no address **/Overdose of psychotropic drugs./** Clinical pearls. Psychiatric Annals. 3(5):6-7,11, 1973.

Clinical manifestations of tricyclic antidepressant poisoning are briefly described, and various methods to prevent or control cardiovascular and other complications that may result in death are stressed. These include use of pyridostigmine to counteract the anticholinergic properties of the drugs or physostigmine, which has the advantage of both central and peripheral effects to counteract the central and peripheral anticholinergic properties of the drugs, as well as the ability to lower heartrate and improve cerebral function. Another useful agent is is dilantin, which prevents both cardiac and cerebral arrhythmias. At present there is no effective way of increasing the metabolism or the elimination of tricyclic drugs from the body; the one positive step is use of activated charcoal or ion exchange resins in gastric lavage mixture to absorb drug remaining in the bowel. In addition, the myocardial injury produced by the drugs may persist beyond the period of coma and must be suspected for as long as a week. Finally, since it appears that adrenergic and direct myocardial toxicity, as well as the anticholinergic effect, may play a crucial role in tricyclic arrhythmia, Glucagon has been used as a cardiotonic agent with some success.

176238 Greenberg, Lawrence M.; McMahon, Shirley A.; Deem, Michael A. Dept. of

Psychiatry, University of California, School of Medicine, Davis, CA 95616 **Side effects of dextroamphetamine therapy of hyperactive children.** Western Journal of Medicine. 120(2):105-109, 1974.

Dextroamphetamine, prescribed in the treatment of hyperactive children, was associated with significant personality deterioration in five of 26 treated cases. Discontinuance of the drug and, in some cases, substitution of others was followed by lessened symptoms of disorganization or of toxicity. It is concluded that children being treated with psychostimulants should be kept under careful observation for untoward reactions. 6 references. (Journal abstract)

176432 Bourgeois, M.; Lefort, H.; Legros, P. U.E.R. de Psychiatrie, Centre Jean-Abadie, F 33-Bordeaux, France **/Dolichomegacolon induced by neuroleptics among psychiatric patients (memorandum covering 153 cases)./** Dolichomegacolons par neuroleptiques en milieu psychiatrique (Note a propos de 153 cas). Annales Medico Psychologiques (Paris). 1(4):556-565, 1972.

The neuroleptogenic etiology of dolichomegacolon among psychiatric methods are considered, including diet therapy, observation of intestinal rhythm, occupational therapy, surgery and treatment for constipation and colitis. Radiologic examination is suggested as an effective diagnostic method. Patients are classified as to age, length of hospitalization, and treatment modality. 64 references.

176674 Jefferson, James W. University Hospitals, 1300 University Avenue, Madison, WI 53706 **Hypotension from drugs: incidence, period, prevention.** Diseases of the Nervous System. 35(2):66-71, 1974.

The incidence and seriousness of one adverse drug reaction, hypotension, as it affected the adult inpatient population of a psychiatric hospital are investigated. Of the 61 patients studied, during the first 72 hours of drug therapy, postural hypotension was documented in 41%. It is felt that this figure is probably a conservative estimate of the true incidence. Symptomatic reactions occurred in 18% of the patients and were mainly relatively mild complaints such as weakness, dizziness, fatigue, and unsteadiness. Not only has the incidence of drug induced hypotension been shown to be high, but there are marked variations in the way such episodes are recognized and dealt with by the hospital staff. It is concluded that in order to minimize such reactions, a hospital ward should have a unified comprehensive approach to drug therapy; such a program centers around the concept that postural hypotension is the most sensitive index of drug induced hypotension. 12 references.

177392 Hilton, Angela M.; Walsh, David B. University Hospital of South Manchester, Manchester, England **Acute cerebellar disturbance associated with diazepam therapy -- a case report and further investigation.** Clinical Toxicology. 6(4):547-551, 1973.

A case report of acute cerebellar disturbance associated with ingestion of diazepam is presented, and further studies of diazepam metabolism after recovery are described. Examination and investigations failed to reveal hepatic or renal pathology, raising the possibilities of idiosyncracy to small doses of the drug or of administration of a larger dose than stated. Drug tolerance levels were within the normal limits, and failure to produce clinical features exhibited previously suggested that the patient unwittingly took a larger dose than she could recall. 14 references.

177393 Cate John C.; Jatlow, Peter I. Dept. of Laboratory Medicine, Yale University School of Medicine, New Haven, CT **Chlordiazepoxide overdose: interpretation of serum drug concentrations.** Clinical Toxicology. 6(9):553-561, 1973.

A retrospective study of 60 cases of chlordiazepoxide (Librium) overdose was performed to establish the clinical significance of drug concentrations. Concentrations ranged from 0.1to 6.6mg/100ml. Seventy seven percent of the ingestions involved other drugs in addition to chlordiazepoxide, most often barbiturates and ethanol. Following ingestion of chlordiazepoxide alone, drowsiness or stupor occurred with concentrations above 2.0mg/100ml, but coma was not seen. Results suggest that if patients cannot be aroused following chlordiazpoxide ingestions, regardless of the serum concentration, another drug or cause of coma should be sought. However, chlordiazepoxide probably contributes in cases of mixed ingestions. 14 references. (Author abstract modified)

177394 Bailey, David N.; Jatlow, Peter I. Department of Laboratory Medicine, Yale University School of Medicine, New Haven, CT **Methyp-**

rylon overdose: interpretation of serum drug concentrations. Clinical Toxicology. 6(4):563-569, 1973.

Serum drug concentrations obtained in 10 cases of methyprylon (Nodular) overdose were examined in a retrospective correlation of clinical findings with drug concentrations and findings in other reported cases. Methyprylon concentrations in serum ranged from 1.7to 8.8mg/100ml. Concentrations above 3mg/100ml were associated with unconsciousness whether or not other drugs were ingested. Six of the 10 cases invloved at least one other drug in addition to methyprylon. All patients recovered quickly with supportive therapy only. Hemodialysis was not required in any of the cases. 12 references. (Author abstract modified)

177395 Gard, H.; Knapp, D.; Walle, T.; Gaffney, T.; Hanenson, I. Department of Pharmacology, Medical University of South Carolina, Charleston, SC **Qualitative and quantitative studies on the disposition of amitriptyline and other tricyclic antidepressant drugs in man as it relates to the management of the overdosed patient.** Clinical Toxicology. 6(4):571-584, 1973.

The disposition of tricyclic antidepressant drugs, in particular gastric secretion and biliary and urinary excretion, was studied as it relates to the treatment of overdose patients. The binding of these drugs by activated charcoal was studied in vitro in human gastric juice. In the cases studied, continuous aspiration of gastric secreted drug for 24 hours removed amounts comparable to that removed by initial lavage and considerably greater than that removed by urinary excretion. These results, together with measures of biliary excretion, suggest that repeated gastric and intraduodenal administration of charcoal may be helpful in the treatment of tricylcic antidepressant drug overdose. 13 references. (Author abstract)

177396 Ostrenga, James A. Pharm Chem Laboratories, 1848 Bay Road, Palo Alto, CA 94303 **Methaqualone -- a Dr. Jekyll and Mr. Hyde?** Clinical Toxicology. 6(4):607-609, 1973.

Dangerous and addictive qualities of methaqualone are discussed which have led to reevaluation of the substance's status under the Drug Abuse Control Act. Pharmacological properties and psychophysiological effects of methaqualone are described. Although the hypnotic effects of the drug are similar to barbiturates, its sensual effects indicate that it acts on a different central nervous system site. The synergistic action of methaqualone and alcohol is stressed, with most methaqualone related deaths attributed to drug overdoses and mixture with alcohol.

177452 Tennant, Forest S., Jr. Department of Preventive and Social Medicine, UCLA School of Medicine, Los Angeles, CA 90024 **Complications of methaqualone-diphenhydramine (Mandrax) abuse.** British Journal of Addiction (London). 68(4):327-330, 1973.

Complications resulting from methaqualone-diphenhydramine (Mandrax) abuse are described on the basis of observed effects in 67 American soldiers requiring hospitalization for drug abuse. Adverse reactions included overdose, psychotic reaction, psychological or physical dependence and violent reactions. Of the two drugs in the combination of methaqualone-diphenhydramine, methaqualone appears primarily responsible for adverse effects. 6 references. (Author abstract modified)

177710 Sathananthan, Gregory L.; Gershon, Samuel. Neuropsychopharmacology Research Unit, Department of Psychiatry, New York University Medical Center, 550 First Ave., New York, NY 10016 **Imipramine withdrawal: an akathisia-like syndrome.** American Journal of Psychiatry. 130(11):1286-1287, 1973.

The case histories of three patients who developed an akathisia like syndrome after the abrupt withdrawal of imipramine are presented. A possible link between this phenomenon and dopamine turnover in the central nervous system is discussed. 14 references. (Journal abstract)

178019 Tanaka, Ryoichi; Ogata, Motoi; Honda, Osamu; Kinokuni, Yutaka; Okamoto, Yoshiaki; Yaga, Shun; Sakaoka, Umeko; Sanada, Hiroshi; Teraoka, Masatoshi. Department of Neuropsychiatry, Sapporo Medical College, Japan **Effects of PG-501 on parapyramidal system syndrome induced by psychotropics.** Medical Consultation and New Remedies (Tokyo). 9(3):641-646, 1972.

The effect of PG-501 on parapyramidal system syndrome induced by administration of psychotropic drugs was studied, based on an experiment in which 30 mainly schizophrenic patients treated with various psychotropic drugs and experiencing serious side-effects, including Parkinsonism, akathisia and diskinesia were treated

with PG-501 (increasing dose from 15 to 60mg/day for 4 weeks, orally). The results show this drug was remarkably effective and eliminated all the symptoms in 20 patients (66.7%) and noneffective in only six patients (20.0%). PG-501 was particularly effective in those Ss exhibiting tremor (83%).

180063 Hartl, O.; Dejaco, R.; Friedl, H.; Purgyi, P. Barmherizigen Bruder Hospital, A-4020, Linz, Germany **/EKG alternations in infusion treatment with tricyclic antidepressive drugs./** EKG-Veranderungen unter Infusionsbehandlung mit trizyklischen Antidepressiva. Pharmakopsychiatrie Neuropsychopharmakologie (Stuttgart). 5(1):20-25, 1972.

EKG changes caused by intravenous or oral administration of clomipramine and trimpramine to depressed patients are reported. The changes primarily consist of nonspecific ST-T wave alterations with no difference in the drugs used. The alterations are more frequent during intravenous therapy and in the group of patients over 50 years of age. 16 references. (Author abstract)

180070 Eckmann, F. no address **/Extrapyramidal disturbances brought on by neuroleptics./** Neuroleptisch bedingte extrapyramidale Storungen. Basel, Karger, 1971. 73 p.

Neuroleptics are discussed in relation to the etiology of extrapyramidal disorders. This side-effect may be mitigated by associating the treatment with antiparkinsonian medication, a conclusion already reached. The scope of this research is to determine the extent of disturbances attributable to neuroleptics, to the psychosis, or to the constitution, in the broad sense set forth by Kretschmer. A total of 1885 patients were studied, 809 (42.9%) of whom were given neuroleptics. Extrapyramidal disturbances developed in 241 (12.8%) of those treated and in 189 (10.0%) of those not treated. The findings that extrapyramidal disturbances, contrary to previous observations, were not related to sex, age, associated physical ailments, cerebral lesions, and posology of a single application or total medication, is of particular interest.

180147 Haider, Ijaz. Welsh National School of Medicine, Whitchurch Hospital, Cardiff CF 4, England **Drug abuse -- overdose and recovery.** Pakistan Medical Forum (Karachi). 6(8):19-25, 1971.

Overdose and recovery after drug abuse in 127 cases are discussed. The drugs involved were generally barbiturates (50 cases), Mandrax (23 cases), nitrazepam or Mogadon (19 cases), tricyclic antidepressants (10 cases), and miscellaneous drugs (25 cases). All patients except four survived. Continuous EEG monitoring was employed and the findings were related to the clinical assessment of depth of coma. Grade Seven abnormality or complete electrical silence lasting up to 28 hours was seen in 15 cases, 11 of whom made full clinical recovery. Thirteen patients transferred to psychiatric care after acute drug poisoning were also studied for periods of weeks by all night electrophysiological recordings. The day or two after recovery of consciousness, the patients may still be under the influence of an anxiety producing drug. In the subsequent days, they may develop delirium or epileptic phenomenon. Slow wave sleep (Stages 3 and 4) was very low or absent in the first recovery weeks, whereas REM sleep was increased during the early weeks of brain recovery following the chemical injury. 5 references.

180148 Haider, Ijaz. Dept. of Psychiatry, Univ. of Edinburgh, England **Acute nitrazepam (Mogadon) poisoning: an electroencephalographic study.** Pakistan Medical Forum (Karachi). 5(12):19-26, 1970.

The clinical efficacy of a nonbarbiturate hypnotic (nitrazepam, Mogadon) is reviewed and 19 cases of acute nitrazepam poisoning are reported. Electrophysiological parameters were recorded during acute nitrazepam poisoning. All patients were conscious and made full clinical recovery. Their temperature varied between 35.6degrees C and 37.8degrees C. Minor EEG abnormalities were observed: three patients were EEG grade two and the remaining 16, EEG grade one. 16 references. (Author abstract)

180149 Haider, Ijaz. Dept. of Psychiatry, Univ. of Edinburgh, England **Electroencephalographic changes in acute phenobarbitone poisoning.** Pakistan Medical Forum (Karachi). 5(10):13-25, 1970.

Electrophysiological changes in 13 patients (5 men and 8 women) with acute phenobarbitone poisoning are presented. All made full clinical recovery. One patient was treated with forced alkaline diuresis and the remainder received intensive supportive therapy. Rate of elimination of the phenobarbitone from the body was very slow.

One of the patients had higher serum phenobarbitone levels when she became conscious than at the time of admission. This may be due to rapid development of tolerance during her period of unconsciousness. It is evident that cases of phenobarbitone poisoning, even when they are fit clinically, still may have high serum phenobarbitone levels and, therefore, should not be discharged from the medical care in such a state. Continuous EEG monitoring revealed spontaneous shifts where large slow waves with little superimposed fast frequency would alternate with faster frequencies with abundant superimposed drug induced fast activity. 3 references. (Author abstract modified)

180152 Haider, Ijaz. Dept. of Psychiatry, University of Edinburgh, England **The electroencephalographic changes in acute barbiturate poisoning.** Pakistan Medical Forum (Karachi). 6(2):11-39, 1971.

Continuous EEG monitoring was employed in a study of 50 cases of acute barbiturate poisoning admitted to Edinburgh Royal Infirmary. The EEG as seen in the initial record was classified into grades one to seven. EEG grades one and two were associated with a conscious patient showing drowsiness; EEG grades three and four patients were unconscious but responded to painful stimulation. Grades five, six, and seven were associated with deep coma and could not be distinguished clinically. Grade seven, an isoelectric record, totally unresponsive to all stimuli, lasting up to 28 hours was seen in eight cases. All these eight patients made a full clinical recovery. A significant correlation was found between the EEG grade of coma and the clinical assessment of depth of coma, the body temperature, the duration of coma, and also the serum levels of long acting barbiturates. 29 references. (Author abstract modified)

180243 Ananth, Jambur V.; Ban, Thomas S.; Lehmann, Heinz E. Division of Psychopharmacology, McGill Univ., Quebec, Canada **Nicotinic acid-induced systemic lupus erythematosus.** Indian Journal of Psychiatry (Madurai). 14(3):351-355, 1972.

Systemic Lupus Erythematosus (SLE) induced by nicotinic acid is reported in a series of 11 patients. A case of probably drug induced SLE was encountered in the Douglas Hospital associated with the administration of nicotinic acid. A case report of a 43-year-old single man is presented. He was diagnosed as schizophrenia, schizoaffective type. He was treated with various phenothiazine preparations equivalent to 900mg to 1200 mg of phenothiazine units daily. About 6 weeks later, he was placed on nicotinic acid 3200mg and chlorpromazine 600mg daily. About 3.5months later, he was diagnosed as having SLE, possibly drug induced. Ten chronic schizophrenic patients each received 3200mg of nicotinic acid daily combined with various phenothiazine and antidepressant medications. Immunological studies revealed that six out of the 10 had positive antinuclear antibodies. 31 references.

180247 Ananth, J. V. Dept. of Psychiatry, McGill Univ., Montreal, Quebec, Canada **Avoidance of adverse reactions.** Indian Journal of Psychiatry (Madurai). 14(3):293-298, 1972.

Methods for avoidance of adverse reactions to drugs are presented. A program of adverse reaction reporting by active surveillance method was implemented at the Douglas Hospital during 1968. The majority of reported reactions occurred in multiple drug administration. The types of adverse reactions included: neurological, psychiatric, gastrointestinal, dermatological, and cardiovascular and hematological reaction. During 1969, a total of 524 patients manifested 730 adverse reactions. Most adverse reactions occurred in patients 30 years old. Patients with drug dependence manifested the highest incidence of adverse reactions followed by patients with affective psychosis and psychosis with organic brain syndromes, schizophrenia, and patients with paranoid states. With modern pharmacotherapy the safety of the patients depends on the physician's knowledge and skill in using the drugs effectively with minimal adverse reaction. Education at various levels, including the public and the physicians is needed. 13 references.

180248 Menon, M. Sarada; Ramachandran, V. Madras Medical College, Madras, India **Trifluperidol -- therapeutic response and extrapyramidal symptoms.** Indian Journal of Psychiatry (Madurai). 14(3):289-292, 1972.

The possible relationship between therapeutic response and extrapyramidal symptoms was examined in 100 schizophrenics. In the controlled clinical trials of trifluperidol on schizophrenic patients, rating scales were employed to assess the clinical improvement and extrapyramidal symptoms. About 62% of the patients on trifluperidol developed extrapyramidal symptoms. Parkin-

sonism was commonest. Dystonic reaction and akathisia occurred in a few. Sex ration, age distribtuion, and time interval of extrapyramidal side-effects were studied. No significant correlation between therapeutic response and gross extrapyramidal symptoms was noticed. The concept of neuroleptic threshold and the mechanism of production of extrapyramidal symptoms is discussed. 11 references. (Author abstract modified)

180700 Ventouras, K; Dick, P; Buri, P. Laboratories de Pharmacie Galenique de l'Universite de l'Ecole-de-Medecine, CH-1211 Geneva 4, Switzerland **/A few Galenic method to prolong the action of lithium sulfate./** Etude d'une nouvelle forme galenique a action prolongee de sulfate de lithium. Schweizerische Medizinische Wochenschrift. 103(24):878-881, 1973.

In order to eliminate the plasma peaks of lithium and reduce the number of daily intakes of the drug, a sustained release dosage form of a lithium salt which shows very good bioavailability was developed. Absorption kinetics of solutions of lithium carbonate and sulphate are compared with those of the new dosage form in patients treated by a single dose and in patients under continuous treatment, with particular attention to the side-effects. Results are discussed. 36 references. (Author abstract modified)

181377 Koizumi, Shinsuke; Takahashi, Yukio; Aono, Tetsuhiko; Maruko, Kazuo; Kumashiro, Hisashi. Department of Neuropsychiatry, Fukushima Medical College, Fukushima, Japan **Chronic meprobamate intoxication and photomyoclonic response.** Fukushima Medical Journal (Fukushima). 22(1/2):9-13, 1972.

Chronological observations following electroencephalographic (EEG) examinations are detailed for a 23-year-old man who showed abstinence symptoms of chronic meprobamate intoxication. The study showed that the transient photomyoclonic response (PMR) was relatied to the abstinence symptoms of meprobamate intoxication and the low threshold of abnormai EEG. The correlation of the PMR appearance and the low convulsive threshold and so called 'Durchgangs-Syndrome' is discussed. 20 references. (Journal abstract modified).

181395 Jarvik, Lissy F. Veterans Administration Hospital, Brentwood, Los Angeles, CA **Psychotropic drugs and cytogenic effects.** Psychopharmacology Bulletin. 10(1):65-66, 1974.

Whether imipramine produces detectable chromosome damage was studied. Preliminary data from in vitro studies failed to reveal readily demonstrable chromosome damage; however, imipramine did inhibit cell growth, inhibition increasing with drug concentration.

16 METHODS DEVELOPMENT

175332 McGlashan, Thomas. Psychopharmacology Research Branch, National Institute of Mental Health, 5600 Fishers Lane, Rockville, MD **The documentation of clinical psychotropic drug trials.** Rockville, MD, NIMH, 1973. 130 p.

Documentation of clinical drug trials that typically involve evaluations of new psychotropic compounds is presented. Topics include principles of documentation of research studies, review of the content and use of standard reporting forms to record demographic information, clinical symptomatology, laboratory values, and drugs given with therapeutic and toxic effects; explanation of the various statistical methods involved in processing data from clinical trials; and intensive study of a sample of computer generated output, focusing on various ways of displaying data for quick and reliable interpretation. The information processing system was developed by the biometric laboratory of a large university, in cooperation with the Psychopharmacology Research Branch of the National Institute of Mental Health.

176871 Bailey, Leonard C.; Shroff, Arvin P. College of Pharmacy, Rutgers University, New Brunswick, NJ **Simultaneous analysis of a 1,5-benzodiazepine and its metabolite in blood and urine by spectrodensitometry.** Research Communications in Chemical Pathology and Pharmacology. 7(1):105-118, 1974.

The simultaneous quantitation of 7-trifluoromethyl-l-methyl-5-phenyl-lH -1,5-benzodiazepine-2,4-(3H,5H)-dione and its N-demethyltated metabolite using fluorescence quenching spectrodensitometry is described. Schoeffel Model 3000 Spectrodensitometer with a photomultiplier tube detector was used for transmission measurements. A spectrodensitometic method for determination of a 1,5-benzodiazepine tranquilizer and its primary metabolite in blood or urine is described. After extraction from the biological fluids with toluene and subsequent TLC, fluoresence quenching was used to detect the compounds. Quantitation was accomplished by a standard curve generated by using norethin-

drone acetate as an internal standard. The method is sensitive to 0.1mcg. of either compound with a relative standard of deviation of 6 to 8%. Plasma and urine data are presented to demonstrate the utility of the method. 16 references. (Journal abstract modified)

177403 Kreuz, David S.; Axelrod, Julius. Payne-Whitney Clinic, New York Hospital, 525 East 68 St., NYC, NY 10021 **Amphetamine in human plasma: a sensitive and specific enzymatic assay.** Science. 183(4123):420-421, 1974.

A sensitive and specific enzymatic isotopic method of determining plasma amphetamine concentrations in man is described. The assay is based on the transfer of the tritiated methyl group of S-adenosyl-L- (methyl-3H)methionine to amphetamine in the presence of a partially purified N-methyltransferase from rabbit lung. With this assay, as little as 10 nonograms of amphetamine per milliliter of plasma can be accurately determined. The concentrations of d and l-amphetamine in the plasma after 20 to 30 milligrams of the drug have been ingested by humans are reported. 11 references. (Author abstract)

177645 Hablitz, John J.; Borda, Robert P. Neurophysiology Dept., Methodist Hospital, Houston, TX 77025 **The effects of Dalmane (flurazepam hydrochloride) on the contingent negative variation.** Electroencephalography and Clinical Neurophysiology (Amsterdam). Supplement 33:317-320, 1973.

The effects of Dalmane, a new hypnotic agent, on the contingent negative variation (CNV) was studied in six normal subjects. A small but reliable reduction in click evoked responses and CNV amplitude was noted when predrug and postdrug baseline recordings were compared with those obtained during drug administration. Possible applications of CNV to clinical research are discussed. 6 references. (Author abstract modified)

180256 NIMH/Psychopharmacology Research Branch; George Washington University Biometric Laboratory. NIMH, 5600 Fishers Lane, Rockville, MD 20852 **The documentation of clinical psychotropic drug trials: sample output package.** Rockville, MD, NIMH, 1973. 132 p.

A sample output package to provide documentation of clinical trials involving psychotropic compounds is presented. The package represents an example of the computer generated output developed by The George Washington University Biometric Laboratory and the Early Clinical Drug Evaluation Unit of the Psychopharmacology Research Branch, NIMH. It has been compiled for teaching purposes and is to be used in conjunction with the workbook entitled, 'The Documentation of Clinical Psychotropic Drug Trials.'(Author abstract modified)

181315 Masuda, Tetsuro. Department of Legal Medicine, Kumamoto University Medical School, Kumamoto, Japan **Medico-legal studies on isolation and identification of hypnotics by thin layer chromatography (TLC) -- Report 1. Thin layer chromatography of hypnotics and tranquilizers.** Journal of the Kumamoto Medical Society (Kumamoto). 46(2):105-118, 1972.

Separation and identification of several kinds of hypnotics by thin layer chromatography (TLC) were investigated. The most suitable solvent system and color reagents for detection of barbiturates, nonbarbiturates and tranquilizers were sought. The most suitable solvent system and color reagent for barbiturates were acetone/ethylenechloride (15:85) and 1% HgN03, respectively. Nonbarbiturates were identified by various solvent systems and color reagents. The most suitable solvent system for the identification of tranquilizers was acetone/cyclohexane/ethyl alcohol (4:4:2). The most suitable means to obtain color spots was the spraying of 5% AgN03/ammonia (9:1) followed by the spraying of 4% p-dimethylaminobenzaldehyde. 24 references. (Journal abstract modified)

17 MISCELLANEOUS

175072 Kido, Matazo. Tokyo Medical and Dental University, Tokyo, Japan **Relationship between response to low pentamethylenetetrazol administration and personality of juvenile offenders and their repeated crimes.** Clinical Electroencephalography (Osaka). 13(9):652-656, 1971.

A biological or cerebral physiological disposition to convulsion under low levels of pentamethylenetetrazol administration in a population of juvenile delinquents is discussed. Personality disorders evident in repeated offenses or murder are highly correlated to convulsive susceptibility under this drug. 22 references.

175251 Mester, Roberto. no address **Psychiatrists' reactions to their patients' refusal of drugs.** Israel Annals of Psychiatry and Related Disciplines (Jerusalem). 10(4):373-381, 1972.

The reactions of a group of psychiatrists to refusal by their patients of prescribed psychotropic drugs are described, classified and analyzed in terms of motivation and effect on the patients. The impression was that refusal of the drug, which implied a rejection of the doctor himself, would arouse aggressive impulses which would form the center of the motivational system underlying the studied reactions. It is concluded that self-analysis by the doctor administering psychopharmacological treatment can help greatly in transforming his behavior into a useful instrument in the success of the chemical treatment. 8 references. (Author abstract)

175284 Saulle, Richard D. 173 Colonial Parkway North, Yonkers, NY 10710 **Psychopharmacology of the cannabinoids.** Psychosomatics. 14(6):352-354, 1973.

The psychopharmacology of the cannabinoids is reviewed based on studies of man and animals. The fundamental concepts of cannabinoid biochemistry are discussed, particularly its biologic activity, areas of accumulation and effects on mouse behavior. Further, cannabis induced modification of EEG in man and animals is considered, as are alterations of physiologic and neural homeostasis. The broad social acceptance of cannabinoids requires that cannabis derivatives be given a special degree of investigational priority. 12 references.

175537 Schmidbauer, Wolfgang; vom Scheidt, Jurgen. no address /**Manual of intoxicating drugs.**/ Handbuch der Rauschdrogen. Munich, Nymphenburger, 1971. 260 p. DM 22.00.

Aspects of drug research and a classification of intoxicating drugs is presented. The fascinating interrelationships between consciousness and matter, drugs, psyche and society, causing harm as well as inspiration, are discussed. An alphabetic glossary dealing with the history, use, mechanism of action of the individual drugs, is included, as are articles on the sociological, psychological and medical psychopharmacological aspects of intoxicating drugs.

175620 Sethna, Katie J. Gen. Ass. Bldg, D. N. Road, Bombay-1, India **Use and abuse of drugs in psychiatry.** Bombay Hospital Journal (Bombay). 13(1):22-25, 1971.

Use and abuse of drugs in psychiatry are discussed. A brief classification of drugs used to treat psychiatric patients is presented. Drugs are classified as follows: psycholeptics or sedatives which subdue mental activity or alertness, subdivided into major tranquilizers or neuroleptics, minor tranquilizers, and hypnotics; psychoanaleptics of two varities, true mood elevators and stimulants; and psychodysleptics or psychotomimetics. 3 references.

175762 Sarges, Reinhard. Medical Research Laboratories, Pfizer, Inc., Groton, CT 06340 **1-Aminotetralines -- CNS agents and alpha-blockers.** In: Abstracts of Papers, American Chemical Society (abstract MEDI 38). Chicago, 166th ACS National Meeting, August 26-31, 1973.

Synthesis of a series of 1-aminotetralines and their effects were reported in a paper presented at the 166th Meeting of the American Chemical Society. None of the compounds, unlike various tricyclic neuroleptic drugs, exerted pronounced neuroleptic activity in animals. Certain members of this novel series exhibited an unusual array of biological activities. Resolution of racemic aminotetralines resulted in a clear cut separation of biological activities: tetrabenazine reversal and anticataleptic effects were characteristic for S isomers, while suppression of CER and alpha blocking properties were retained by R isomers. Systematic modification studies were carried out

to explore the influence of other structural parameters on the pharmacological profile and to optimize the pharmacokinetic properties of these drugs. (Journal abstract modified)

175862 Tobias, Lester L.; MacDonald, Marian L. Jefferson County Mental Health Center, Lakewood, CO **Withdrawal of maintenance drugs with long-term hospitalized mental patients: a critical review.** Psychological Bulletin. 81(2):107-125, 1974.

The advisability of drug withdrawal for hospitalized mental patients is discussed. Effects of long-term drug maintenance, including undesirable side-effects, unexplained deaths, mounting costs, problems in drug-state learning, transfer to the nondrug state, and questionable utility, are studied. Methodological flaws that pervade the drug literature are discussed, and drug withdrawal studies are reviewed with methodological considerations. It is felt that the conclusion of the majority of these studies, that withdrawal contributed to deterioration, is not warranted because of frequently repeated design errors. 156 references. (Author abstract modified)

175872 Campbell, Magda. New York University Medical Center, 550 First Avenue, New York, NY 10016 **Biological interventions in psychoses of childhood.** Journal of Autism and Childhood Schizophrenia. 3(4):347-373, 1973.

A review of available drug therapy treatments of childhood psychoses is presented with comments on efficacy based on the author's experience. Mention of earlier forms of biological organic treatment (psychosurgery, insulin, and electroconvulsive therapies) is made. With a focus on drug therapy, prominence is given to major tranquilizers, lithium, and hormones. Information is presented on hypnotics, anticonvulsants, sedatives, stimulants, antidepressant drugs, minor tranquilizers, hallucinogens, L-dopa, and vitamins. It is suggested that no specific drug is available for the treatment of any diagnostic category. Available drugs are effective in reducing such symptoms as insomnia, hyperactivity, impulsivity, irritability, disorganized behavior, psychotic thought disorder, and types of aggressivity. The need for uniformity in classifying child psychoses is stressed because of its potential in predicting responses to specific drugs. 156 references. (Author abstract modified)

175914 Hollister, Leo E. Stanford University School of Medicine, Palo Alto, CA **Clinical use of psychotherapeutic drugs.** Springfield, Ill., Charles C Thomas, 1973. 192 p.

The use of drugs in the treatment of patients with emotional disorders is examined. Consideration is given to: antipsychotic drugs in schizophrenia and other psychoses; antimanic drugs in affective disorders, with emphasis on the limitations and promise of lithium carbonate; antidepressant drugs and their role in the entire approach to depressed patient management; antianxiety drugs, with focus on their prudent use rather than their medical overuse; drug use in treating emotional disorders of children; and drugs used for treating various organic brain syndromes, mental deficiency, alcoholism, and drug abuse. Each class of drugs is considered in relation to the chemical and pharmacological differences among its members, pharmacological properties, and pharmacokinetics as they relate to their clinical use, specific clinical indications, general principles of use, use in combination with other drugs, and their side-effects and toxicology. 241 references.

176438 Peron-Magnan, J.-C. no address **/Psychopharmacology and geriatrics./** Psychopharmacologie et geriatrie. Paris, These, 1971.

Proper management of psychotropic drugs is discussed with respect to their use where children and the elderly are involved. Practical solutions to their use in geriatrics are presented. Drugs are grouped and discussed accordingly. Hypnotics are discussed in terms of their posology and the degree to which they can be tolerated by the elderly. Tranquilizers are discussed at length, and products found to have an anodyne effect on elderly patients are noted. Antidepressants, because of their high tolerance, are particularly recommended for use. Cerebral vasodilators are discussed in brief. Principal products that should be used in geriatrics, rules for their use, and necessary precautions are outlined.

176597 Thiessen, Paul N.; Cook, David A. Dept. of Pharmacology, Univ. of Alberta, Edmonton 7, Alberta, Canada **The properties of 3,4-methylenedioxyamphetamine (MDA). I. a review of the literature.** Clinical Toxicology. 6(1):45-52, 1973.

A review of the literature of 3,4-methylenedioxyamphetamine (MDA) is presented. The drug is a

powerful central stimulant which may possess hallucinogenic properties when administered in high doses. The chemistry, pharmacology and human studies are reviewed. Little is known about the physiological effects of acute dosage of MDA. Death in humans may lie in the hypertension induced hemorrhage or cardiac arrest. Fatal dosages are unknown. 31 references. (Author abstract modified)

176676 Evenson, Richard C.; Altman, Harold; Cho, Dong Won; Sletten, Ivan W. no address **Simple algorithms for predicting psychotropic drugs assigned to psychiatric inpatients.** Diseases of the Nervous System. 35(2):80-83, 1974.

The ability of simple algorithms, primarily diagnostic, to assign classes of psychotropic drugs to psychiatric inpatients in agreement with actual clinical decisions was investigated. Overall agreement (hit rates) ranging from 48% to 65% were found across four major drug groups: major tranquilizer, antidepressant, minor tranquilizer, and no psychotropic drug. These hit rates may be compared with multivariate formulae developed in earlier studies that achieved hit rates ranging from 62% to 77%. Agreement among clinicians (about 70%) appears to be the limiting factor in most studies of this type. 15 references. (Author abstract)

176926 Rees, W. Linford. Department of Psychological Medicine, St. Bartholomew's Hospital, London EC1, England **New horizons in psychopharmacology.** Proceedings of the Royal Society of Medicine (London). 65(9):813-818, 1972.

Recent developments in the area of neuroleptic, tranquillosedative, and central nervous system stimulants and tricyclic antidepression drugs are briefly reviewed, stressing the usefulness of these compounds in treating various psychiatric disorders, as well as delineating their chemical structure and possible contraindications. The neuroleptics depress operant behavior and cause reduction in spontaneous activity and response to external stimuli and are useful in treating overactivity, agitation, impulsiveness, aggression, hallucinatory behavior, and delusions. They may be classified into phenothiaxines, rauwolfia alkaloids and benzoquinolizines, thioxanthines, butyrophenones, diphenyl butyl piperidines, dibenzothiazepines, and benzamides. Tranquillosedatives are used in treating anxiety and include chlordiazepoxide, diazepam, nitrazepam, oxazepam, medazepam, and flurezepam. CNS stimulants and biogenic amines increase wakefulness, stimulate activity and cause temporary elevation of mood and include amphetamines, phenmetrazine, pipradol, methylphenidate. Monomaine oxidase inhibiting drugs also stimulate CNS activity. Tricyclic antidepressants can be classified according to their clinical effects: sedative, anxiolytic action; stimulating, drive increasing action, and effect on depressed mood itself. 27 references.

177063 Suzuki, Yoshio. Department of Oral Surgery, School of Dentistry, Tohoku University, Japan **The problems of the psychopharmacological treatment of psychosomatic diseases -- the anesthesiologic approach.** Journal of Japanese Psychosomatic Society (Tokyo). 10(6):365-368, 1970.

The significance of psychotropic drugs as precursory drugs prior to surgical operations is discussed. Woodridge, Saklad and the American Anesthetic Association's classification of surgical risk or physical status of patients before surgical operation, the psychophysiological characteristics of preoperative patients, and types of psychotropic drugs which can be used as precursory drugs and their effects are considered. The significance of the preoperative interview is also discussed. 7 references.

177066 Nishizono, Masahisa. Department of Psychiatry, Kyushu University School of Medicine, Japan **Some problems in the psychopharmacological treatment of psychosomatic disease.** Journal of Japanese Psychosomatic Society (Tokyo). 10(6):359-364, 1970.

The application of psychotropic drugs in psychosomatic illness is discussed. Psychotropic drugs and placebo are about equally effective in relieving somatic anxiety, but are not useful in relieving somatic symptoms. Anxiolytic, autonomic and antidepressive drugs are commonly used in psychosomatic cases. Benzodiazepam derivatives and other drugs inducing unusual side-effects should be avoided as they may aggravate the patient's depression or anxiety. Physical or psychological drug dependence may arise in harcissistic patients or when drug treatment is not accompanied by psychotherapy. 11 references.

177190 Matsumoto, Yutaka. Chiba University School of Medicine, Japan **Topics in psychiatry: psychotropic medicine.** Clinic All-Round (Osaka). 19(7):1364-1369, 1970.

Psychotropic drugs and their application are discussed. The history of development of psychotropic drugs, classification and chemical synthesis of psychotropic drugs, and mechanism of action are considered. 12 references.

177676 Ananth, J. V. Department of Psychiatry, St. Mary's Hospital, Montreal, Quebec, Canada **Exacerbation of psychopathology during treatment: etiology.** Comprehensive Psychiatry. 14(6):563-568, 1973.

An examination of the cause of exacerbation of psychopathology during treatment is presented. Exacerbation of psychopathology during treatment can be divided into the following categories: 1) psychosis due to insufficient treatment; 2) paradoxical psychosis; 3) pendular psychosis; 4) intentional psychosis produced by chronic drug ingestion in high dosage; 5) withdrawal psychosis; 6) drug interaction psychosis due to combined administration of drugs. Even though undesirable effects occur in spite of precise use of medication, most cases of exacerbation of psychopathology related to drug therapy can be prevented. Prevention, prompt recognition, and treatment depend on the physician's skill and vigilance.

177699 Manheimer, Dean I.; Davidson, Susan T.; Balter, Mitchell B.; Mellinger, Glen D.; Cisin, Ira H.; Parry, Hugh J. P. O. Box 5007, Berkeley, CA 94715 **Popular attitudes and beliefs about tranquilizers.** American Journal of Psychiatry. 130(11):1246-1253, 1973.

In a nationwide survey of the extent and nature of psychotherapeutic drug use, respondents were also questioned about their knowledge of tranquilizers and their attitudes toward the use of these drugs in general and in specific situations. The survey revealed similarities of attitudes across demographic subgroups. Although respondents believed in the efficacy of tranquilizers and were willing to condone their use in some specific circumstances, they also had doubts about their long-term effects and about the morality of using them. Doubts about the morality of using tranquilizers were associated with traditional stoic values. 5 references. (Author abstract)

177782 Engelhardt, David M. no address **Pharmacologic basis for use of psychotropic drugs: an overview.** New York State Journal of Medicine. 74(2):360-366, 1974.

An overview of psychotropic drugs in clinical practice is presented with an assessment of the present state of the art of psychopharmacotherapy of adults. Psychotropic drugs are classified into three groups on the basis of the target symptoms that they are presumed to attack: (1) antipsychotic or neuroleptic agents, (2) antidepressant or thymoleptic agents and (3) antianxiety or anxiolytic agents. Each of the three categories is surveyed as to effectiveness in given diagnostic categories. It is felt that the search for the etiology of the major psychiatric disorders will continue and may bring researchers closer to a holistic view of the psychoses and more rational and effective multidisciplinary approaches. Research involving the schizophrenic patient is discussed. It is hoped that the underlying process of schizophrenia will be remedied and that resocialization will take place; drugs alone cannot resolve the problems of the schizophrenic. 9 references. (Author abstract modified)

178002 Saito, Masami. Kansai Ika Daigaku, Japan **Psychotropic drugs.** Nippon Rinsho (Osaka). 28(Special Issue):48-49, 1970.

Types of psychotropic drugs and their effects are discussed. Types of hypnotics, neuroleptics, and tranquilizers and their effects are considered.

178029 Vencovsky, E. Dukelska 69, Plzen, Czechoslovakia **/Possible mutual therapeutic combination of psychopharmaceuticals./** Moznosti vzajemne terapeuticke kombinace psychofarmak. Ceskoslovenska Psychiatrie (Praha). 69(4):231-235, 1973.

The need to follow basic management procedures in clinical pharmacopsychiatry by prescribing one drug in specific doses for a specific period is discussed. The clinical picture as a whole must be considered, not just the nosology of the psychic disorder, when selecting treatment. Combinations of drugs may be indicated, but a distinction must be made between drug combinations that involve the use of several drugs at the same time, and therapeutic combinations utilizing biological therapeutic procedures, electroconvulsive therapy, for example, and drugs. Advantages and disadvantages of using drug combinations to combat side-effects are pointed out. It is concluded that the principle to be followed in psychiatry is to use one drug at a time, despite persuasive therapeutic effects attributed to combinations.

178044 no author. no address **Role of associative learning in feeding behavior.** Final Report, NIMH Grant MH-16423, 1972, 17 p.

The role of associative learning in feeding behavior was investigated. In research relevant to alcoholism, it was found that chemical aversion therapy has been more successful in the treatment of alcoholism than any other treatment except for Alcoholics Anonymous. Lithium has been used successfully in this respect. In delayed reward of a conventional motor response experiment, it was found that the traditional Hull-Spence theory of delayed reinforcement which still dominates learning theory has been definitely disproven. The only valid theory at present is the interference approach. In experiments concerning sensory preconditioning in flavor toxicosis learning, sensory preconditioning (SPC) occurs if a light is followed by a tone and then the tone is paired with shock. Backward conditioning does not occur in ordinary SPC experiments unless the intertrial interval is so short that the possibility of forward conditioning over the intertrial interval cannot be precluded.

178109 Eun, Chamroen Sam. Sonn-Mam Hospital, Takhmau, Cambodia /**Psychotropic drugs in Cambodia.**/ Les psychotropes au Cambodge. Indonesian Psychiatric Quarterly (Djakarta). 3(3/4):29-36, 1970.

An overview of psychotropic drugs in Cambodia is presented. The use of psychotropic drugs in the treatment of mental illness in a psychiatric hospital is described against the background of earlier treatment by healers, sorcerers, and quacks. Neurotic or reactive depressions are shown to have responded favorably to antidepressants (imipramine or Amitriptyline) in association with anxiolytic drugs. Use of the latter is increasing annually. Psychostimulants are rarely used and hallucinogens have not yet appeared on the scene. Major tranquilizers modify the course of psychoses and chronic deliriant states. Difficulties are encountered with patients with persecution delusions and who experience side-effects with neuroleptic treatment. Psychiatrists look forward to new products which will enable them to bring about better human conditions.

178127 Robin, Stanley S.; Bosco, James J. Dept. of Sociology, Western Michigan Univ., Kalamazoo, MI 49001 **Ritalin for school children: the teachers' perspective.** Journal of School Health. 43(10):624-628, 1973.

The teacher's perspective on the drug Ritalin (methylphenidate hydrochloride) is reviewed. Study is made of questions concerning the teacher's information about Ritalin, teacher attitudes toward the drug, and professional behaviors reported by a teacher when encountering a child with behavioral problems. Relationships between attitudes and knowledge and other characteristics of teachers such as number of past experiences with children known by the teacher to be taking Ritalin are explored. It is noted that overall the attitudes of teachers toward the use of Ritalin are cautiously favorable. While teachers often may have a pupil taking Ritalin, it is uncommon for teachers to have specific and accurate information about characteristics of the drug. Teachers are divided between a passive role, an active and cooperative role, and uncertain responses. It is recommended that teachers and physicians communicate more frequently, and that school systems institute behavior modification - drug education programs for staff. 8 references.

178189 Moamai, N. Service d'oligophrenie de l'Hopital Saint-Jean-de-Dieu, Montreal, Canada /**Psychiatric care: drugs, therapist, community.**/ Sur les soins psychiatriques (medicaments, therapeute, communaute). Vie Medicale au Canada Francais (Quebec). 2(9):855-856, 1973.

Aspects of psychiatric care including drugs, therapists and community, are analyzed. The pharmacodynamic role of drugs in psychiatry is that of a modifying agent, moderating, restraining, and regulating at the level of the central nervous system. The therapist acts on the fragmentation of the ego, on the derangement of the relational system, and on the pathogenic stress medium to create a livable equilibrium within the environment that forms the patient. Classical psychiatry is oriented towards mental health community centers for treatment of psychiatric patients in their environment, to help them with immediate problems when faced with stress and to avoid their slipping into chronic illness. Guidelines determining the role of the therapist and the power of drugs in psychiatry, emphasizing psychological and extrapharmacological dimensions, are defined. 3 references.

178655 Nishikiori, Tohru. Kyoto Prefectural Rakunan Hospital, Kyoto, Japan **Psychiatric treatment: what comes after pharmacological therapy?** Koyto Igaku-kai Zasshi. 18(1):53-55, 1968.

The importance of community psychiatry in the future of psychiatry is discussed. Insulin and electric shock treatment have been replaced by psychopharmacology in the past 10 years, and psychopharmacology in turn has facilitated the socialization of psychiatry, which had an isolated and unsocial nature. Remission of psychiatric symptoms is achieved much earlier and so is rehabilitation of mental patients. Many mental patients who return to society, however, often experience relapse and fail to adjust themselves to social life due to lack of community awareness of mental illness. The necessity for establishment of a rehabilitation and socialization system for mental patients in the community is stressed. 8 references.

178677 Karon, Bertram P.; VandenBos, Gary R. Michigan State University, East Lansing, MI **Long term consequences of experience, medication, and psychotherapy for schizophrenic patients. (Unpublished paper).** East Lansing, Michigan State University, 1974. 8p.

Long-term consequences of therapist experience, medication and psychotherapy were examined for schizophrenic patients. Ss were 35 patients randomly assigned to three treatment groups: 1) psychoanalytic therapy of an active variety without medication; 2) psychoanalytic therapy of an ego analytic variety with medication; 3) a comparision group that underwent routine treatment of medication and supportive therapy. Within the first two groups, four Ss were seen by an experienced therapist, the rest by inexperienced therapists under supervision. The treatment period was concluded after 20 months. Results show that Ss who received psychotherapy spent half as much time in the hospital as did those receiving medication and supportive therapy, women were hospitalized for shorter periods of time than men, therapist experience was a critical variable, and differences in technique were not significant unless treatment was conducted by inexperienced therapists. 10 references. (Author abstract modified)

178695 Sinnett, E. Robert; Wampler, Karen S.; Harvey, William M. Kansas State University, Lawrence, KA **Marihuana -- a psychedelic drug?** Psychological Reports. 34(1):47-53, 1974.

Dimensions of the drug experience derived from judgements by experienced drug users were combined to separate marihuana and psychedelic drugs into two classes. The marihuana substances were judged as calming as opposed to exciting, relatively safer, and less potent than psychedelic drugs. These findings and others indicate that marihuana may be more similar to sedative, depressant, and hynotic drugs than to psychedelic drugs. Some superiority in correct classification was found for a nonlinear discriminant function over a linear discriminant function. 19 references. (Author abstract)

179983 Garattini, Silvio; Goldin, A.; Hawking, F.; Kopin, I. J.; Schnitzer, R. J. Istituto di Ricerche Farmacologiche, 'Mario Negri', Milano, Italy **Advances in pharmacology and chemotherapy.** New York, Academic Press, 1973. 380 p. Vol. 11.

Literature on recent advances in pharmacology and chemotherapy is reviewed. The section on monoamine oxidases examines the versatility of catalytic properties and possible biological functions. The method of physicochemical activity relationships as it is used in the prediction of pharmacological activity and the design of drugs is discussed. Cyclic adenosine 3',5'-monophosphate and estrogenic stimulation of uterine metabolism is discussed. Semisynthetic penicillins are examined. Chemotherapy in the control of chicken coccidiosis is discussed. Antiviral drugs are discussed in terms of the technical feasibility of treating virus diseases with drugs and the design of antiviral screens. The chemotherapy of anaplasmosis, babesiasis, and theileriasis is examined. An index is given. 1114 references.

180102 Kawakami, Takeshi; Kaneko, Tsuguo. Suginami Kumiai Hospital, Japan **What is technique in psychiatric treatment?** Journal of Japan Hospital Association (Tokyo). 32(3):106-123, 1973.

Psychiatric treatment since the development of psychotropic drugs is criticized. Since psychotropic drugs appeared on the market, diagnostic techniques in psychiatry have been degraded and psychiatrists have mainly paid attention to elimination of psychiatric symptoms. Although psychotropic drugs may eliminate psychiatric symptoms, they also may induce loss of volition and hypoactivity in patients. The necessity for psychotherapy, milieu therapy, and rehabilitation therapy at mental hospitals and halfway homes is stressed.

180298 Kho, Tjok Khing. Dept. of Psychiatry, Faculty of Medicine, Univ. of Indonesia, Djakar-

ta, Indonesia **Preliminary experiences with the treatment of some mental cases utilizing an enzyme combination.** Indonesian Psychiatric Quarterly (Djakarta). 3(3/4):223-230, 1970.

The effect of enzymes in the treatment of organic brain syndrome was studied in 200 patients for 7 years. The first combination of enzymes included: citro-genase-lipase complex (8000 units), Tyrosinase (400 Units), and Aminoxidase (4000 Units). The second combination of enzymes consisted of: Glutamine synthetase (5000 Units), Aceto-co-A kinase (5000 Units), and enzymes of oxidative phosphorylation (5000 Units). During the first week, each patient received daily injections, alternately with 2ml of the first and second enzyme combination. After 1 week, the enzyme preparations were given alternately three times weekly for 3 months; if there was a response in the patient, maintenance dosage of the enzyme preparation was given once weekly during 2 months and afterwards once monthly during at least a year. If there was no response in the patient, the thrice weekly method was continued for another 3 months. The average number of injections given was approximately 50. No side-effects occurred in the course of 10,000 injections. Of the 200 patients, 40 patients reacted excellently; 66 patients showed good reaction; 64 patients reacted fairly; 30 patients showed no improvement; and 26 patients died. 26 references.

180307 Tanaka, Kiyoshi. Faculty of Medicine, Kyushu University, Japan **Characteristics of benzodiazepine tranquilizers.** Fukuoka Acta Medica (Fukuoka). 63(3):87-93, 1972.

Literature on the psychopharmacological characteristics of benzodiazepine tranquilizers is reviewed. Types of benzodiazepine derivatives, hypnotic action, antiepileptic action, muscular relaxation action, tranquilizing action and autonomic nervous system regulatory action are considered. Brain locations affected by this type of drug are also discussed. 49 references.

180320 To, Duong Hiep. Hopital Psychiatrique, Bien Hoa, Viet Nam **Status of psychotropic medication in Viet Nam.** Indonesian Psychiatric Quarterly (Djakarta). 3(3/4):92-95, 1970.

The history of psychotherapy in Viet Nam, particularly regarding psychotropic medication, is discussed. The short supply of psychiatrists and the prevalence of witchcraft and superstition have severely hampered psychotherapy in Viet Nam. With the introduction of phenothiazine in 1962, the quality increased. Nurses have been trained to use these medications so that larger areas can be covered. Chlorpromazine, reserpine, antidepressives and minor tranquillizers are used extensively. Admissions are not down and more trained psychiatrists are needed to followup and supplement drug therapy.

180321 Ou, George Ta-Wei. Dept. of Psychiatry, Castle Peak Hospital, Hong Kong **Psychotropic medication in Hong Kong.** Indonesian Psychiatric Quarterly (Djakarta). 3(3/4):75-80, 1970.

The status of psychotropic medication in Hong Kong is reported in relation to the development of the Mental Health Service over the years. A short history of psychotherapy in Hong Kong is included. The mental patient population has quintupled since 1930 to its present total around 76,000, or an admissions rate of two per every 10,000 population. Psychotropic medication has allowed more admissions of considerably shorter duration. Unfortunately, the reliance on drugs has reduced the amount of real psychotherapy necessary to effect a real rehabilitation. 5 references.

181146 Petti, Theodore A.; Kane, Francis J., Jr.; Lipton, Morris A. Dept. of Child and Adolescent Psychiatry, New York University Medical Center, New York, NY 10016 **Problems in teaching psychopharmacology.** Psychosomatics. 14(6):326-330, 1973.

The teaching of psychopharmacology in an apparently typical medical school is evaluated systematically with regard to the prescription of psychotropic drugs and the appropriateness of the prescription, dosage, and the diagnosis of the patient considering the presented symptoms. Performance of medical students, who generally have an extremely brief clincial experience and a minimal investment in psychiatry, is compared with that of second year psychiatric residents. It was found that: 1) diagnosis and chart material correlated poorly for 50% of students records and for almost 25% of resident records; 2) almost 10% of the charts were so poor as records that they could not be evaluated; 3) almost one quarter of the times medication was used by the students it was the wrong medication and in more than half the cases, the dosage was incorrect; 4) residents used medication correctly only 52% of the time, and dosage was correct only half the time; and 5) there was significant evidence of polypharmacy. The data indicate the need for continued educa-

tional endeavor in the area of psychopharmacology throughout a residency program. 11 references.

181638 United Nations Social Defence Research Institute. United Nations Social Defence Research Institute, Rome, Italy **Psychoactive drug control: issues and recommendations.** Rome, UNSDRI, 1973.

Suggested methods and programs for controlling psychotropic drug abuse are presented. Emphasis is on the development and application of international collaborating agreements for drug control. Some data assisting in predicting or assessing drug use outcomes and correlates are presented. Typical laws and programs in the national or international field are listed. The implementation of classification and control schemes and the economic basis for the assessment of costs and benefits are considered. Some of the major unresolved issues are presented. It is conceded that uncertainty in drug classification is common. Legislators should consider as many alternatives as possible. Recommendations for further action are offered. Evaluation and need for factual bases are also stressed.

181713 Balter, Mitchell B.; Levine, Jerome; Manheimer, Dean I. Psychopharmacology Research Branch, National Institute of Mental Health, Rockville, MD 20852 **Cross-national study of the extent of anti-anxiety/sedative drug use.** New England Journal of Medicine. 290(14):769-774, 1974.

National samples of respondents in nine Western European countries were asked identical questions about their use of antianxiety/sedative drugs during the past year and about their general attitude toward tranquilizers. The proportion of persons who used antianxiety/sedative drugs on one or more occasions varied from 17% in Belgium and France to 10% in Spain. In almost every country the percentage of females who had used antianxiety/sedative drugs was approximately twice that of males. Persons 45 years of age and over were overrepresented among drug users in all countries in relation to their presence in the national population. The rank order of the countries on attitude toward tranquilizers was poorly correlated with rank order on use rates. However, within each country there was a sharp difference in attitude between users and nonusers. Independent data place the U.S. in a middle position among the nine countries surveyed on use of antianxiety/sedative drugs. 6 references. (Author abstract).

182106 Shibuya, Takeshi; Endo, Takahiko. Department of Pharmacology, Tokyo Medical College, Tokyo, Japan **Automatic recording of animal behavior and its analysis.** Japanese Journal of Pharmacology (Kyoto). 22(Supplementum):93, 1972.

At the 45th meeting of the Japanese Pharmacological Society, the automatic recording of animal behavior and its analysis was reported. This apparatus is designed for metrical, objective and continual evaluation of animal behaviors by means of three dimensional factors and digital analysis of the findings. By the use of the apparatus, it was found that tranquilizers, antidepressants and other CNS drugs respectively have a unique mode of action different from one another. (Author abstract modified)

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